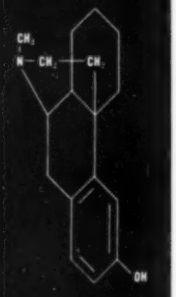
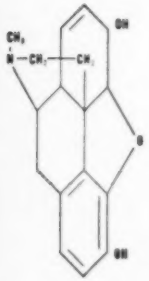
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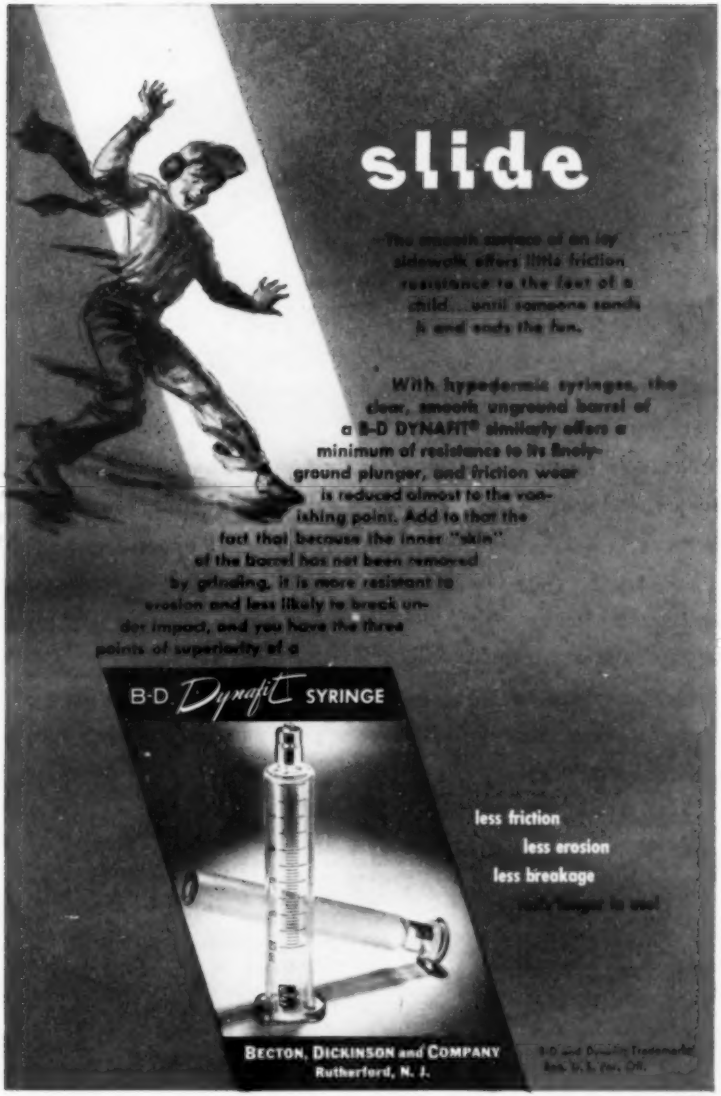
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DROMORAN

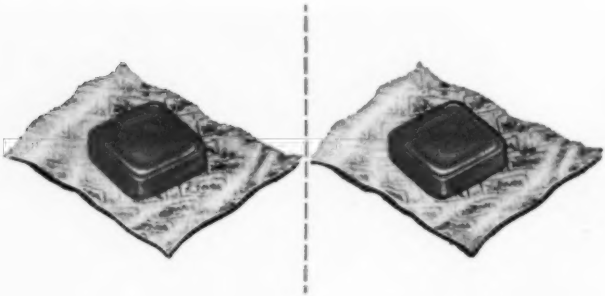
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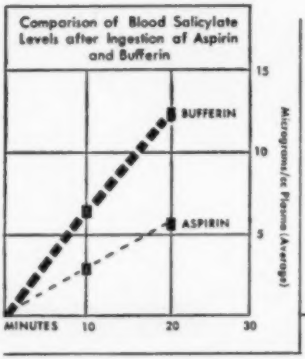
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1. Gitman, L., and Kaplowitz A.: Use of diethylstilbestrol in complications of pregnancy. New York State J. Med. 50:2823: 1950.
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3. Karnaky, K.J.: Am. J. Obsts. & Gynec. 58,622. 1949.

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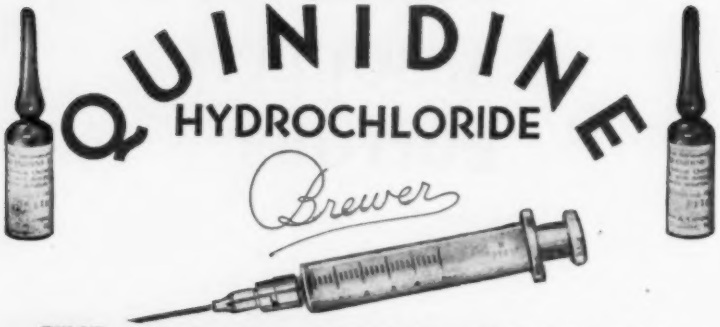
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1. Sturnick, M. I.; Riseman, J. E. F.; and Sagall, E. I.: Studies on the Action of Quinidine in Man: J. A. M. A. 121:917 (March 20) 1943.
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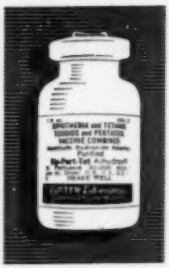
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1. Fremont, R. E.: Rimmerman, A. B., and Shaftel, H. E.: Postgrad. Med. *10*:216, 1951.
2. Rimmerman, A. B., et al: Am. Pract. & Digest Treat. *2*:168, 1951.

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IN THE YEARS AFTER 1215, civilization and common sense had occasion to celebrate a victory over human stupidity. It was during this period in history that the enlightened nations abolished the medieval ordeal by fire and the ordeal by water as a test of character, endurance, innocence or guilt.

In an interesting record of a soldier's life in the British Army during the clamorous time of the Napoleonic wars,[1] the writer in his diary recounts how he was vigorously dosed before the entire regiment with "three ounces and a half of the bitter gall Epsom salts, and two hours knapsack drill in double quick time to open my back door."

Today, "violent purging such as that produced by 15 to 30 grams (½ to 1 ounce) of magnesium sulfate or 30 cc. (1 ounce) of castor oil, is rarely wise and should be deplored," in the opinion of Philip W. Brown,[2] because "this sweeping out of the bowel is unphysiologic and . . . normal bowel movement cannot occur for perhaps two or more days after such an insult."

The discovery of the laxative properties of phenolphthalein made it possible to relieve constipation by gentle peristaltic stimulation over several days with a single dose, resulting in softening and regulation of the stools.[3] Krantz and Carr[4] find that along with other advantages, the mild cathartic action of phenolphthalein makes it one of the most popular cathartic drugs. Extensive clinical experience has shown phenolphthalein to be safe in a wide range of dosage.[5]

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1. The Letters of Private Wheeler. Houghton Mifflin, 1952.
2. P. W. Brown: Current Therapy, 1950. Saunders; page 203.
3. T. Sollmann: A Manual of Pharmacology. W. B. Saunders Co., 1948; page 177.
4. J. C. Krantz, Jr. and C. J. Carr: The Pharmacologic Principles of Medical Practice. Williams & Wilkins, 1951; page 377.
5. M. L. Blatt, F. Steigmann, and J. M. Dyniewicz: J. Pediat. 22:719, June, 1943.

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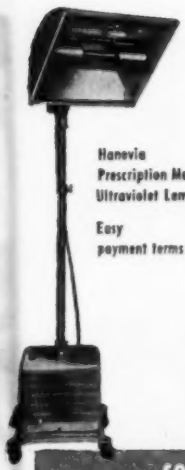
Samples and literature on request

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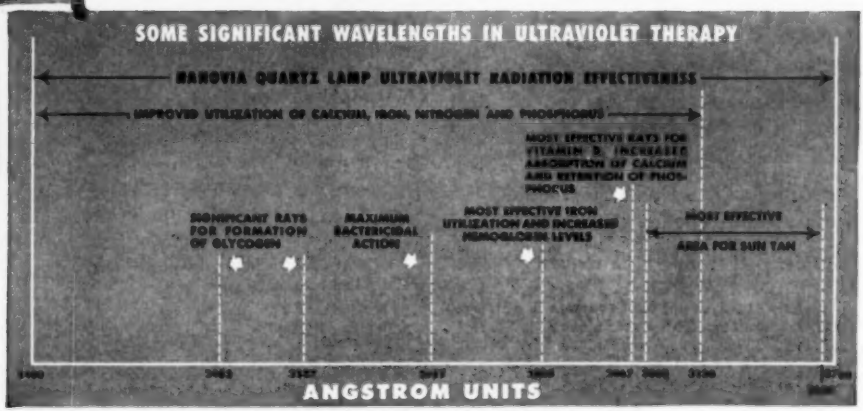
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1. *Seley, S. A.: Am. J. Dig. Dis. 13:258 (July) 1946.* 2. *Rossien, A. X.: Rev. of Gastroenterol. 16:34-52 (Jan.) 1949.* 3. *Rossien, A. X. and Victor, A. W.: Am. J. Dig. Dis. 14:226-229 (July) 1947.* 4. *Batterman, R. C. and Ehrenfeld, I.: Gastroenterol. 9:141 (August) 1947.*

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LETTERS TO THE EDITOR

This department is offered as an Open Forum for the discussion of topical medical issues. All letters must be signed. However, to protect the identity of writers, who are invited to comment on controversial subjects, names will be omitted when requested.

Replacing Other Journals

"I am pleased to receive your recent letter regarding why I receive MEDICAL TIMES. I hope I may continue to get it. In the last year or two I have found it to be my favorite reader. It has replaced CALIFORNIA MEDICINE, J.A.M.A., and official journal of G. P. to a great extent."

William H. Littleton, M.D.
Fresno, Calif.

Dizziness Refresher

"Your 'refresher' in the August issue of MEDICAL TIMES is excellent.

"I have only one criticism, and that is that as the picture is painted, the perspective emphasizes the textbook approach, rather than that of the patient. This may cause your readers among the internes and younger physicians to ignore the functional disorders such as postural hypotension and localized edema (localized anemia and/or congestion) which may lie at the root of the complaint.

"In other words, I would say that vasomotor instability is responsible for more complaints of 'dizziness' than any of the organic disorders so well delineated in your article.

"Nor is the carotid sinus sensitivity given the prominence that Monroe found

—Concluded on page 44a

If Anemia Therapy Is to Be More Effective It . . .

". . . should provide an abundance of those articles which, according to clinical experience and animal experiment, have been shown best to promote regeneration of blood . . ."[1]

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1. McLester, J. S.: Nutrition and Diet in Health and Disease. Ed. 5. (Philadelphia: W. B. Saunders and Co.) 1949, p. 636. 2. *Ibid.*

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THIAMINE HYDROCHLORIDE	2 mg.
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DISCUSSION

"Protamide has been used successfully for treatment of chickenpox. There was prompt relief of pruritis, fever, discomfort, and definite amelioration and shortening of the disease."*



**Lehrer, H. W.; Lehrer, D. R.; Lehrer, H. G.; Ohio State Med. Jr. (Jan.) 1951.*

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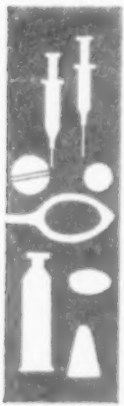
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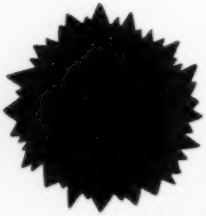
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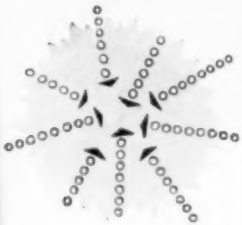
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2. Cutting, W. C.: GP 4:65, November 1951.



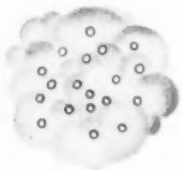
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(Limber, C. R.; Reiser, H. G.; Roettig, L. C., and Curtis, G. M.: Enzymatic Lysis of Respiratory Secretions by Aerosol Trypsin, J.A.M.A. 149: 816-821, (June 28) 1952.

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REFERENCES: 1. American Practitioner and Digest of Treatment, 2:944, 1951. 2. J. Pharmacol. & Exper. Therapy, 87:24, 1946. 3. Ibid, 73:65, 1941. 4. J. Pharmacol. 77:324, 1943. 5. J. Lab. & Clin. Med., 28:603, 1943.

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1. Waters, E. G., and Wager, H. P.: Amer. J. Obstet. & Gyn. 60:885, 1950.



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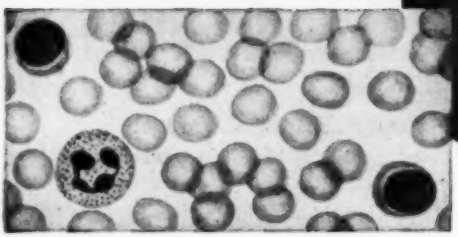
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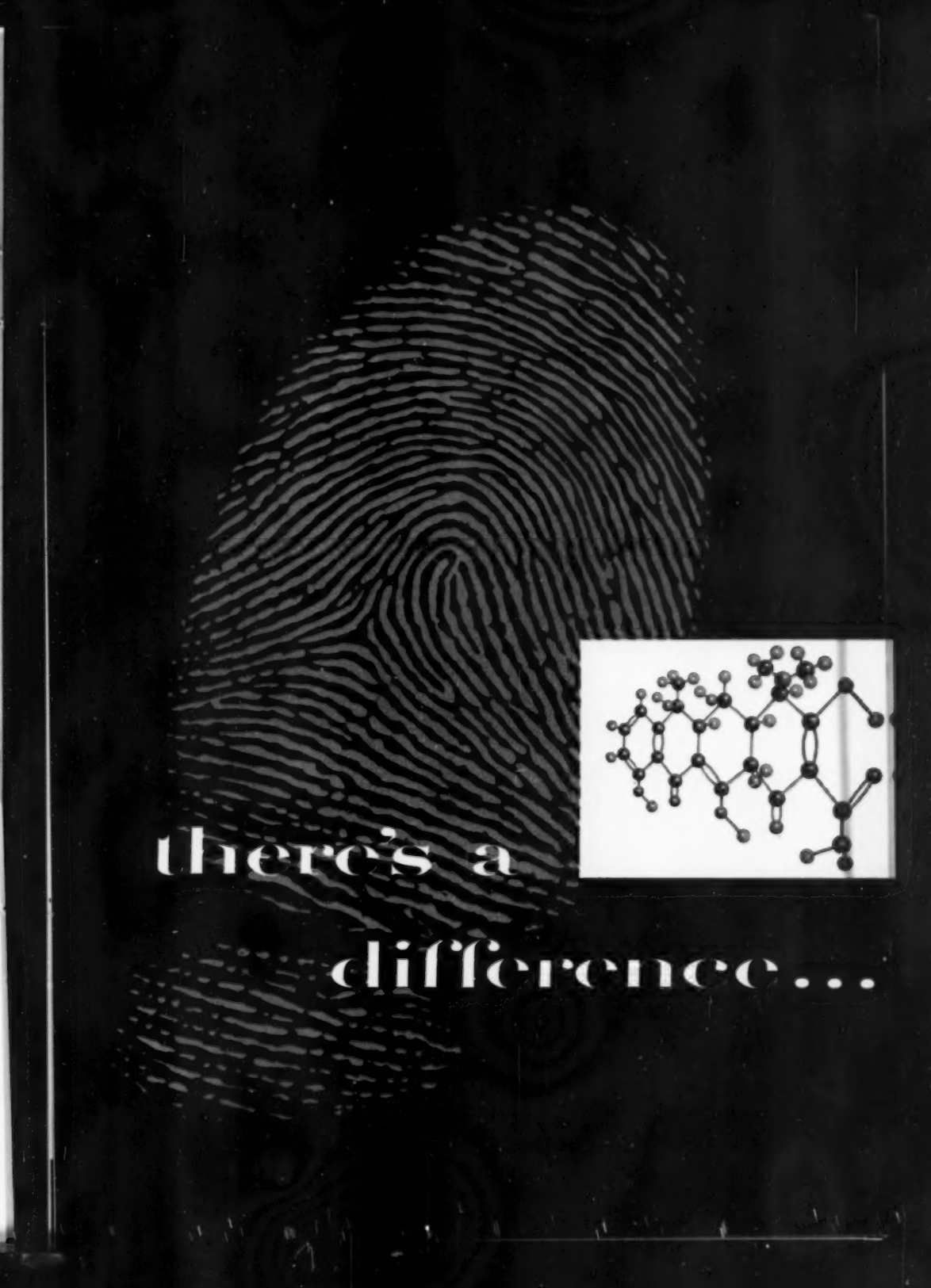
2 OR 3 CAPSULES T. I. D.

Winthrop-Stearns INC.

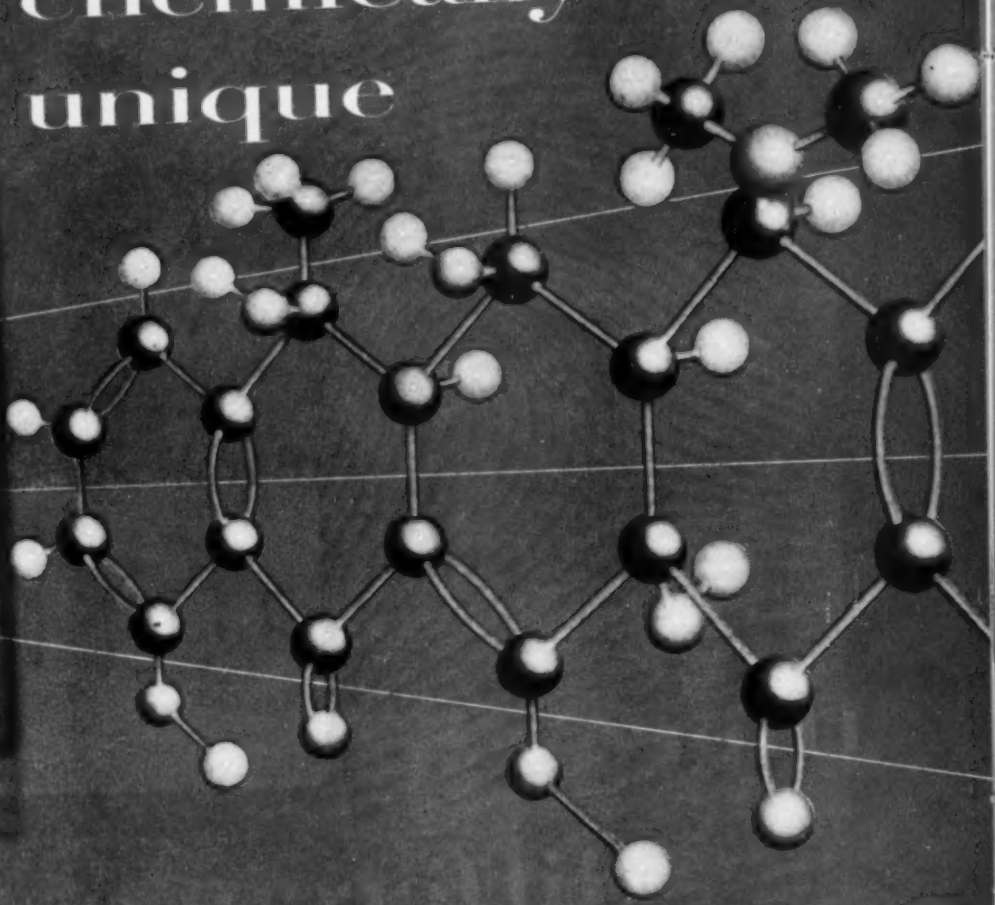
New York 18, N. Y. • Windsor, Ont.

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there's a
difference...

chemically unique



...as shown by the recent discovery of its molecular structure

Pfizer

clinically unexcelled

Terramycin

for TOLERATION

EFFECTIVENESS

PURITY

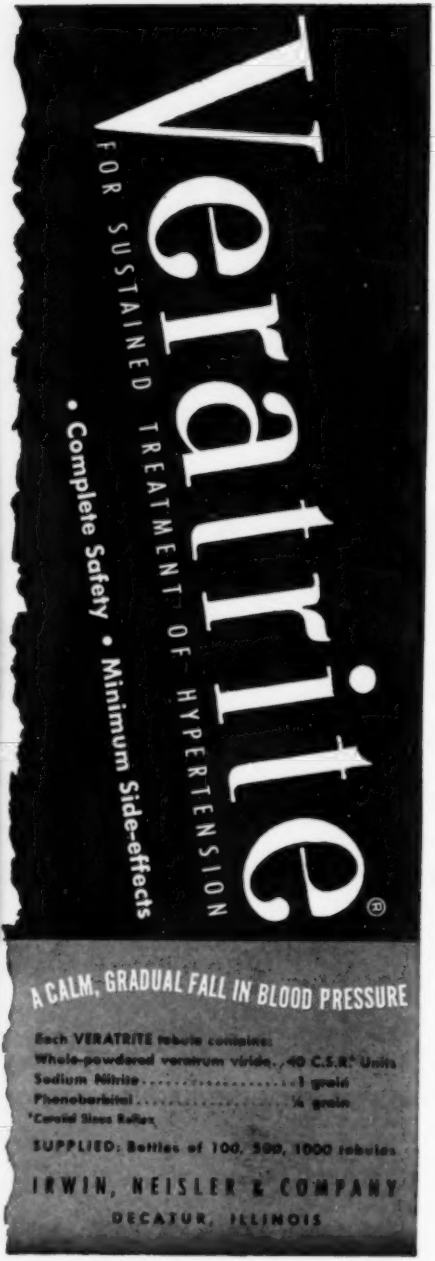
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ANTIBIOTIC DIVISION, CHAS. PFIZER & CO., INC., BROOKLYN 6, N. Y.

world's largest producer of antibiotics

DON'T MISS 

APPEARING REGULARLY IN THE J. A. M. A.



LETTERS TO THE EDITOR

—Concluded from page 28a

in his study of the 7000 case histories in his geriatric clinic at the Peter Bent Brigham Hospital in Boston."

G. H. Hoxie, M.D.
Berkeley, Calif.

Most Practical

"I just want you to know that I consider your magazine the most practical, the most informative and interesting book for the G.P. today. Many thanks. I am indeed pleased to be identified as 1 out of 5."

H. Ameroy Hartwell, M.D.
Weehawken, N. J.

Reprints for the Profession

"I recently received the reprint on 'Low Back Pain' which I requested. I find it to be so well done and so very complete that I am going to make a request which I hope you will please grant me. Will you be good enough to mail me a reprint of each and every different subject which you have on hand for distribution to the profession? I shall value them because they should serve to supply me with up-to-date material on these various matters."

Harry G. Rinzler, M.D.
Passaic, N. J.

"I have received the reprint of 'Low Back Pain' and thank you sincerely for it is the best and most complete monograph on the subject that I have studied in many years.

"Your magazine is most welcome and, unlike most of my magazines, it happens to be one of the few that I read from cover to cover because I find both interesting and instructive articles that are worthy of the time it takes to read them."

Joseph I. A. Thompson, M.D.
Margate City, N. J.



Koagamin Controls Post-Tonsillectomy Bleeding

Spontaneous or postoperative bleeding may be controlled with KOAGAMIN easily and quickly.[1] It has been found especially effective in post-tonsillectomy bleeding for its double action — decreasing coagulation time,[2] and increasing clot resistance even in hemophiliacs.[3]

KOAGAMIN'S direct action on the blood and tissue fluids renders it more useful than vitamin K, effective only when blood prothrombin is low. In such cases, KOAGAMIN is recommended in conjunction with slower-acting vitamin K to effect faster control.

KOAGAMIN®

(An aqueous solution of oxalic and malonic acids for parenteral use)
In 10 cc. diaphragm stoppered vials.
Descriptive literature and comprehensive dosage chart upon request.

THERAPEUTICALLY aids control of bleeding gastric and duodenal ulcers, hematemisis, hematuria, uterine bleeding, the dyscrasias, etc.

PREOPERATIVELY minimizes oozing, assures a clearer surgical field.

POSTOPERATIVELY controls secondary bleeding.

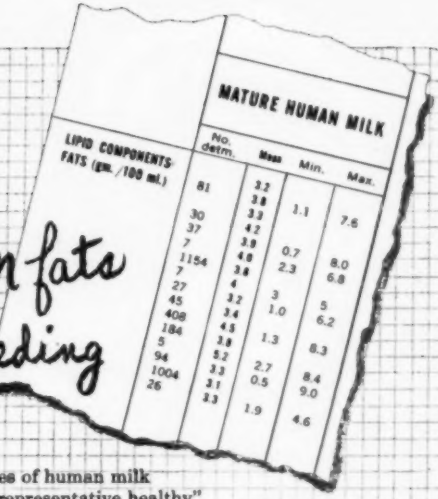
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3. Copley, A. L. and Lalich, J. J. Am. Jl. Med. Sci. 204:665. 1942.

Chatham

Available Through Your Physician's Supply House or Pharmacist

CHATHAM PHARMACEUTICALS, INC. NEWARK 2, NEW JERSEY, U.S.A.

fats...
and figures on fats in infant feeding



LIPID COMPONENTS: FATS (gm./100 ml.)	MATURE HUMAN MILK			
	No. determ.	Mean	Min.	Max.
	81	3.2		
		3.8	1.1	7.6
	30	3.3		
	37	4.2		
	7	3.9	0.7	
	1154	4.0	2.3	8.0
	7	3.6		6.8
	27	4	3	
	45	3.2	1.0	5
	408	3.4		6.2
	184	4.5	1.3	8.3
	5	3.8		
	94	5.2	2.7	8.4
	1004	3.3	0.5	9.0
	26	3.1		
		3.3	1.9	4.6

A breakdown of over 3,000 samples of human milk obtained from hundreds of "representative healthy" mothers,* showing mean fat values, as well as the maximum-minimum ranges.

(From Bull. of the National Research Council, No. 119, January 1950)

the fat content of reliquefied SIMILAC

3.35%, closely approximates the average mean value for well-nourished-mothers' milk.

but the similarity doesn't end there

Qualitatively, the fat of Similac corresponds closely in physical and chemical properties to the fat of mother's milk. The high level of unsaturated fatty acids, the uniformly small globule size and the increased essential fatty acids approximate those of breast milk. Thus Similac, like breast milk, affords easy digestion of fat, good fat retention, and encourages freedom from gastrointestinal disorders and from dermatologic complications due to low essential fatty acid diet.

Similac is available as Powder, 1 lb. tins, and Liquid, 13 fl. oz. tins

* The mother whose nutritional state is below par frequently produces milk with low fat values.[1, 2] In one large series of poorly nourished mothers, the average dropped to 2.9%, with 10% of cases below 2.0%.[1] The fat content of Similac approximates that found in milk of well-nourished mothers. It is consistent and unvarying, always adequate, a fact to remember when breast feeding is not feasible.

Similac is so similar to human breast milk that there is no closer equivalent

1. Muller-Stephann, H., Ztschr. Kinderheilk. 67:495, 1950.
2. Salmi, T.: Acta Paediatrica 32:1, 1944.

A QUARTER CENTURY OF PROGRESS IN INFANT NUTRITION

M & R LABORATORIES
Columbus 16, Ohio



in postpartum breast engorgement...

...estrogen and androgen go together 'like pulley and rope' to provide a dual approach for maximum efficiency. A current trend of opinion is that these two steroids together, as combined in "Premarin" with Methyltestosterone, will have a greater effect on suppression of lactation than either one alone. Excellent results from such therapy have been reported by many clinicians

Ayerst

Ayerst, McKenna & Harrison Limited

New York, N. Y. • Montreal, Canada

"PREMARIN"

with

METHYLTESTOSTERONE

for combined estrogen-androgen therapy

6221

CONSTIPATION*

possibly the

greatest single medical problem

of the patient who is over **40**



In these cases, laxation *alone* isn't enough.

Because constipation in this age group is usually associated with indigestion and biliary stasis.

Prescribe Caroid[R] and Bile Salts with Phenolphthalein to obtain these three beneficial actions:

choleretic action — for an increased flow of bile

digestant action — aids protein and fat digestion

laxative action — gentle laxation with minimal dosage

Supplied — bottles of 20, 50, 100, 500 and 1000 tablets

write for professional samples to

AMERICAN FERMENT CO., Inc. 1450 Broadway, New York 18, N. Y.

*Rehfuss, M. E.: Indigestion, Philadelphia, W. B. Saunders Co., 1943, p. 322

CAROID AND BILE SALTS *tablets*

Specifically indicated in ***biliary dyspepsia and constipation***



new

convenient

ANDROGEN THERAPY

for women

ORETON-M Buccal Tablets

ORETON-M Buccal Tablets containing methyltestosterone dissolved in POLYHYDROL,® a unique solid solvent, provide a more effective and convenient form of male sex hormone. The buccal route permits methyltestosterone to reach the circulation directly. Indicated for definitive relief of menopausal symptoms in special circumstances; for preventing pain of functional dysmenorrhea; and to relieve discomfort of breast engorgement.

Freedom from masculinizing side effects can be expected with recommended dosage of one-half to one and one-half 10 mg. ORETON-M® (Methyltestosterone U.S.P.) Buccal Tablets daily (5-15 mg.).

ORETON-M

buccal tablets

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for Control of Hypertension



Apresoline™

Hydrochloride
(brand of hydralazine hydrochloride)

Apresoline is a relatively safe, *single* antihypertensive drug with no serious untoward reactions, providing benefits in many cases—complete control in some. It is recommended that Apresoline be used in those hypertensive patients who have not been adequately controlled by conventional regimens (diet, mild sedation, rest, etc.). The following important considerations should be of interest in general practice:

Effective in essential hypertension with fixed levels, early malignant hypertension, toxemias of pregnancy and acute glomerulonephritis.

Provides gradual and sustained reduction of blood pressure with no dangerous, abrupt fall on oral administration.

Affords uniform rate of absorption and infrequent dosage adjustments.

Increases renal plasma flow in marked contrast to the decrease associated with other hypotensive drugs.

Side effects often disappear as therapy is continued or can be ameliorated with adjunctive medication.

Produces significant relaxation of cerebral vascular tone.

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in ARTHRITIS
and allied disorders

BUTAZOLIDIN®

(brand of phenylbutazone*)

New...
Non-Hormonal...
Orally Effective...
Synthetic

for relief of pain plus improvement of function

Now available on prescription, BUTAZOLIDIN is a new and potent agent that has yielded outstandingly favorable results in arthritis and other painful musculoskeletal disorders.

On the basis of the first national reports[1-4] BUTAZOLIDIN:

- *Produces therapeutic benefit* in virtually all forms of arthritis and allied disorders such as bursitis and fibrositis.
- *Effectively relieves pain* in approximately 75 per cent of non-gouty cases and in almost 100 per cent of cases of acute gout.
- *Affords functional improvement* ranging up to complete remission in a substantial proportion of treated cases.

A totally new synthetic, BUTAZOLIDIN is chemically unrelated to the steroid hormones. It is orally effective and seldom produces toxic reaction of a serious character. Moderate in cost, BUTAZOLIDIN may be prescribed even for patients of limited means.

*U. S. PAT. NO. 2,562,830

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3. Freyberg, R.; Kidd, E. C., and Boyce, K. C.: Studies of Butazolidin and Butapyrin in Patients with Rheumatic Diseases. Paper read before the Annual Meeting of the American Rheumatism Association, Chicago, Ill., June 6, 1952.
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In order to ensure optimal results and to avoid untoward reactions, physicians are urged to send for the BUTAZOLIDIN brochure or to read the package circular carefully before prescribing.

Geigy

GEIGY PHARMACEUTICALS
Division of Geigy Company, Inc., 220 Church Street, New York 13, New York



The "DRY TREATMENT" OF VAGINITIS

Comforting to the patient, simple and clean to administer, is the "dry treatment" of vaginal leukorrhea, using—

1. **TRYCOGEN POWDER** insufflation in the office; (optional)
2. **TRYCOGEN INSERTS** for home treatment

In trichomonal, monilia, or senile vaginitis, TRYCOGEN acts to destroy the parasitic invaders, relieve the pruritus, and restore the normal vaginal flora.

TRYCOGEN presents sodium thiosulfate, thymol, oxyquinoline sulfate and oil of wormwood in a base of boric acid and starch. Non-irritating; non-staining.

Trycogen Inserts, Boxes of 18 and 100 • Trycogen Powder, 25-gram vials. Also in 8-oz. and 16-oz. containers.

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CHICAGO, ILLINOIS

Control IN ANGINA PECTORIS AND BRONCHIAL ASTHMA



Amnivin

EFFECTIVE

WELL TOLERATED

SAFE

FLEXIBLE

PARENTERAL

ORAL

THE NATIONAL DRUG COMPANY • PHILADELPHIA 44, PA.

MODERN MEDICINALS

These brief resumes of essential information on the newer medicinals, which are not yet listed in the various reference books, can be pasted on file cards and a record kept. This file can be kept by the physician for ready reference.

Acorto Gel, Geo. A. Breon & Co., Kansas City 10, Mo. Long-lasting adrenocorticotropic hormone. **Dose:** As determined by physician, for intramuscular injection. **Sup:** In 5 cc. vials containing 20 and 40 I. U. of the compounds per cc.

Aerosporin Otic Solution, Burroughs Wellcome & Co., Inc., Tuckahoe 7, N. Y. For treatment of ear infections. **Dose:** Three or 4 drops into the previously-cleaned and dried ear canal 3 or 4 times daily. **Sup:** In 10 cc. vials.

Apamide, Ames Co., Inc., Elkhart, Ind. Analgesic-antipyretic. **Dose:** As determined by physician. **Sup:** In bottles of 100 tablets.

Apromal, Ames Co., Inc., Elkhart, Ind. For non-narcotic, non-barbiturate sedation plus analgesia. **Dose:** As determined by physician. **Sup:** In bottles of 100 tablets.

Armazide, Armour & Co., Chicago, Ill. Isonicotinic acid hydrazide for the treatment of tuberculosis. **Dose:** As determined by physician. **Sup:** In bottles of 100 tablets of 50 mg.

Chloromycetin Solution, Parke, Davis & Co., Detroit 32, Mich. Antibiotic. **Dose:** As determined by physician, intravenous. **Sup:** 0.5 Gm. per 2 cc. ampul in boxes of 6.

Cumertilin Tablets, Endo Products, Inc., Richmond Hill 18, N. Y. Mercurial diuretic for oral use. **Dose:** As determined by physician. **Sup:** In bottles of 100 and 1,000 tablets. Also available as the injection in 1 and 2 cc. ampuls.

Dexedrine Spansules, Smith, Kline & French Labs., Philadelphia, Pa. See dosage. **Dose:** Control of appetite in weight reduction—1 before breakfast . . . Depressive states—1 before breakfast; Nocturnal epilepsy—1 at bedtime; Narcolepsy—1 to 3 at breakfast; Alcoholism—1 at breakfast; Post-encephalitic parkinsonism—1 to 2 at breakfast; Nausea and vomiting of pregnancy—1 at breakfast; To dispel drug-induced drowsiness—1 at breakfast. **Sup:** In bottles of 30 and 250 "spansules."

Dodecavite Crystalline, U. S. Vitamin Corp., N. Y. 17, N. Y. In treatment of subacute combined sclerosis, diabetic neuritis, trigeminal neuritis, herpes zoster, tabes dorsalis, peripheral vascular disorders, and certain other neural conditions. **Dose:** One thousand mcg. by intramuscular or subcutaneous injection every 5 to 10 days followed, if necessary, by an injection once or twice a week for another 2 or 3 weeks. **Sup:** In 5 cc. vials.

Drilitol Spraypak, Smith, Kline & French Labs., Philadelphia 1, Pa. In local treatment of common upper respiratory tract disorders. **Dose:** Spray 3 to 4 times in each nostril every 3 hours. Children: ½ the adult dose. **Sup:** In ½ fl. oz. plastic squeeze bottle.

Hexamethon Chloride, Burroughs Wellcome & Co., Inc., Tuckahoe 7, N. Y. New hypotensive agent for the treatment of severe hypertension, including malignant hypertension, and when used parenterally in certain peripheral vascular diseases. **Dose:** As determined by physician. **Sup:** In bottles of 100 tablets (250 mg.) and in 10 cc. vials (40.5 mg. hexamethonium chloride per cc.).

INH, Eli Lilly & Co., Indianapolis, Ind. Isonicotinic acid hydrazide for the treatment of tuberculosis. **Dose:** As determined by physician. **Sup:** In bottles of 100, 1,000 and 5,000 tablets.

—Concluded on page 60a



Prelude to asthma?

not necessarily . . .

Tedral, taken at first sign of attack, often forestalls severe symptoms.

in 15 minutes...Tedral brings symptomatic relief with a definite increase in vital capacity. Breathing becomes easier as Tedral relaxes smooth muscle, reduces tissue edema, provides mild sedation.

for 4 full hours...Tedral maintains more normal respiration for a sustained period—not just a momentary pause in the attack.

Prompt and prolonged relief with Tedral can be initiated any time, day or night, whenever needed without fear of incapacitating side effects.

Tedral provides:

theophylline	2 gr.
ephedrine	⅜ gr.
phenobarbital	⅛ gr.

in boxes of 24, 120 and 1000 tablets

Tedral

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MORRIS PLAINS, NEW JERSEY

announcing

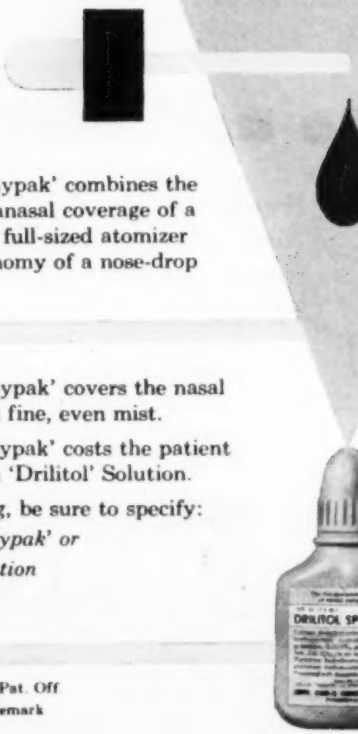
DRILITOL* SPRAYPAK

for intranasal infections

'Drilitol'

now available in 2 forms

'Drilitol Spraypak'
'Drilitol' Solution



'Drilitol Spraypak' combines the superior intranasal coverage of a spray from a full-sized atomizer with the economy of a nose-drop bottle.

'Drilitol Spraypak' covers the nasal mucosa—in a fine, even mist.

'Drilitol Spraypak' costs the patient no more than 'Drilitol' Solution.

In prescribing, be sure to specify:
'Drilitol Spraypak' or
'Drilitol' Solution

*T.M. Reg. U.S. Pat. Off
'Spraypak' Trademark

for intranasal infections

'Drilitol Spraypak'—the new form of 'Drilitol'

Now there are two forms of 'Drilitol', S.K.F.'s widely accepted intranasal preparation: (1) 'Drilitol' Solution, with which you are familiar, and (2) the new convenient form, 'Drilitol Spraypak'.

'Drilitol' contains two antibiotics:

Anti-gram positive gramicidin
Anti-gram negative polymyxin

'Drilitol' also contains:

A vasoconstrictor, Paredrine†
An antihistaminic, thenylpyramine

now available in 2 *forms:*

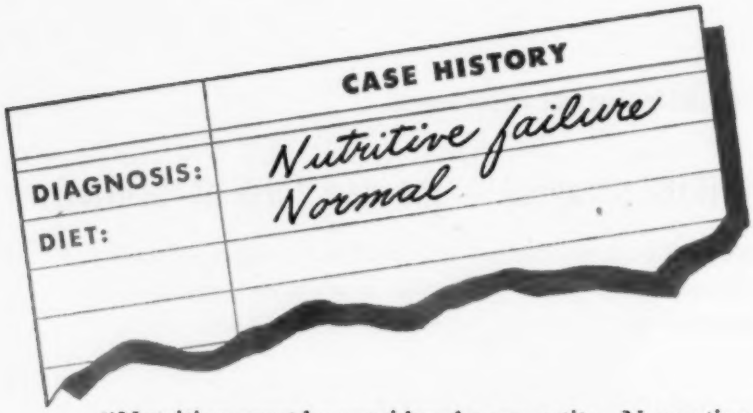
'Drilitol Spraypak'

'Drilitol' Solution

antibiotic, decongestive, anti-allergic

†T.M. Reg. U.S. Pat. Off. for hydroxyamphetamine hydrobromide, S.K.F.

Smith, Kline & French Laboratories, Philadelphia



"Nutrition must be considered as an entity. No particular constituent is more important than another. Each nutrient should be present in its optimum quantity."[1] "If one nutrient is not adequate, this may also interfere with the functioning of other nutrients in the body."[2]

Vitamins, Minerals and Trace Elements each play a specific important role in nutrition.

1. Simonnet, H.: Nutrition in Pregnancy, Canad. M. A. J., 58:556, (June) 1948, p. 60.
2. The Nutrition of Industrial Workers; Second Report of the Committee on Nutrition of Industrial Workers, Food and Nutrition Board, National Research Council. Reprint and Circular Series No. 123. (Washington, D. C.: National Research Council), Sept., 1945, p. 13.

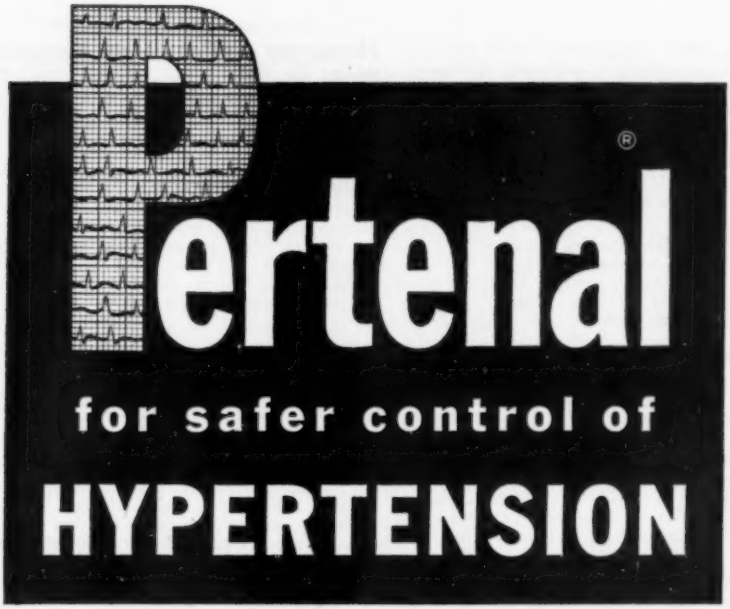
10 Vitamins
11 Minerals and
Trace Elements
All in One Capsule



Viterra

Vitamin A	5,000 U.S.P. Units
Vitamin D	500 U.S.P. Units
Vitamin B_{12}	1 mcg.
Thiamine Hydrochloride	3 mg.
Riboflavin	3 mg.
Pyridoxine Hydrochloride	0.5 mg.
Niacinamide	25 mg.
Ascorbic Acid	50 mg.
Calcium Pantothenate	5 mg.
Mixed Tocopherols (Type IV)	5 mg.
Calcium	213 mg.
Cobalt	0.1 mg.
Copper	1 mg.
Iodine	0.15 mg.
Iron	10 mg.
Manganese	1 mg.
Magnesium	6 mg.
Molybdenum	0.2 mg.
Phosphorus	165 mg.
Potassium	5 mg.
Zinc	1.2 mg.

J. B. ROERIG AND COMPANY
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In PERTENAL the potent vasodilator, mannitol hexanitrate, supplements the hypotensive action of veratrum, allowing the veratrum to take effect at a lower blood pressure level . . . assuring well sustained reduction of pressure, with minimal, *safer* veratrum dosage, *and* prompt relief of headache, dizziness, worry, restlessness, insomnia, gastrointestinal discomforts and other symptoms which often aggravate pressure.

PERTENAL treats the patient as a whole — helps assure *a more comfortable, more tranquil, often longer life.*

Dose: 1 tablet every 4 to 6 hours.
Supplied in bottles of 50, 100 and 500 tablets.

each PERTENAL tablet contains:

Veratrum Viride (standardized extract of the whole drug)	100 mg. (1½ gr.)
Homatropine Methylbromide	2.5 mg. (1/25 gr.)
Mannitol Hexanitrate	30 mg. (½ gr.)
Phenobarbital	15 mg. (¼ gr.)

Comprehensive literature and *samples* on request

CROOKES LABORATORIES, INC. Crookes MINEOLA, NEW YORK

Therapeutic Preparations for the Medical Profession

—Concluded from page 54a

Isolyn, Abbott Laboratories, North Chicago, Ill. As an adjunct to treatment of streptomycin-resistant tuberculosis or tuberculosis not responding to previous therapy. **Dose:** Two to 4 mg. per kilogram of body weight per day. Epileptic patients must be given suitable anti-convulsive agents before and along with ISOLYN. **Sup:** In bottles of 100 and 1,000 tablets.

Milibis, Winthrop-Stearns, Inc., New York 18, N. Y. Now available in bottles of 500 tablets. In intestinal amebiasis. **Dose:** 0.5 Gm. 3 times daily for 7 to 10 days. **Sup:** In bottles of 500 tablets (0.5 Gm. ea.).

Mol-Iron E. M. F., White Laboratories, Inc., Kenilworth, N. J. Anemia therapy. **Dose:** Two capsules 3 times daily. **Sup:** In bottles of 100 capsules.

Neobacin Tablets, Commercial Solvents Corp., New York 16, N. Y. In intestinal amebiasis and specific dysenteries. **Dose:** One to 4 tablets. 4 times daily, depending on age of patient. **Sup:** In bottles of 30 tabs.

Neomycin 0.5 Gm. Tablets, The Upjohn Co., Kalamazoo, Mich. In preparing a patient for gastrointestinal surgery, where it is important to include an agent which is capable of eliminating or suppressing the bacterial inhabitants of the bowel, as well as measures for emptying the bowel of its contents. **Dose:** A single dose of 60 cc. of castor oil is followed immediately by 2 tablets. (1.0 Gm. of neomycin sulfate. This is followed by 2 tablets every hour for 4 doses, then 2 tablets every 4 hours. **Sup:** In bottles of 20 tablets.

Pentids Soluble Tablets, E. R. Squibb & Sons, New York 22, N. Y. Soluble penicillin tablets containing 200,000 units of penicillin G potassium. **Dose:** As determined by physician. **Sup:** In bottles of 12 and 100 tablets.

Phenergan Cream, Wyeth, Inc., Philadelphia 2, Pa. In various itching skin disorders. **Dose:** As determined by physician. **Sup:** In 1.12 oz. tubes.

Phenergan Expectorant With Codeine, Wyeth, Inc., Philadelphia, Pa. For cough associated with the common cold, minor throat irritations or minor infections of the upper respiratory tract. **Dose:** One teaspoonful every 4 to 6 hours. **Sup:** In pint bottles.

Phenergan Lotion with Neocalamine, Wyeth, Inc., Philadelphia 2, Pa. To stop the itching in many skin disorders. **Dose:** As determined by physician. **Sup:** In 4 oz. bottles.

Polysporin Ointment, Burroughs Wellcome & Co., Inc., Tuckahoe 7, N. Y. Bactericidal and bacterostatic activity against all types of surface infections. **Dose:** As determined by physician. **Sup:** Now available in tubes of 1 oz. in addition to the 15 Gram and 1/8 oz. sizes already supplied.

Rubramin, E. R. Squibb & Sons, New York 22, N. Y. Vitamin B-12 therapy. **Dose:** As determined by physician. **Sup:** Now available in 10 cc. vials (100 mg. per cc.).

Talsigel, E. R. Squibb & Sons, New York 22, N. Y. Enteric sulfonamide preparation in diarrheas of non-specific origin, in mild early bacillary dysentery, and the control of exacerbations of ulcerative colitis. **Dose:** Adults, 20 to 50 cc. daily; Infants and children under 40 Kg., 1 cc. daily per kilogram of body weight. **Sup:** In one pint bottles.

Tisin, U. S. Vitamin Corp. (Casimir Funk Labs., Inc. Division), New York 17, N. Y. Isonicotinic acid hydrazide. In streptomycin-resistant cases in the treatment of pulmonary tuberculosis. **Dose:** Adult: 150-300 mg. daily in 2 or 3 divided doses. Children: Calculated on the basis of 3 to 5 mg./kg. body weight. **Sup:** In bottles of 100 and 1,000 scored tablets of 59 mg. and 100 mg. respectively.

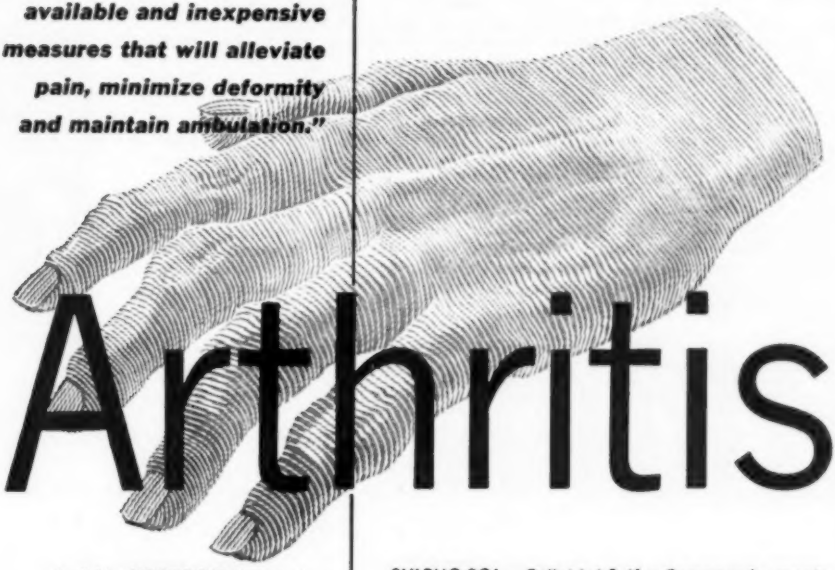
Toryn, Smith, Kline & French Labs., Philadelphia, Pa. Non-narcotic for cough control. **Dose:** As determined by physician. **Sup:** In 4 fl. oz. bottles of the Syrup. In bottles of 25 tablets.

Vergitryl, E. R. Squibb & Sons, New York 22, N. Y. For controlling hypertension. **Dose:** Three tablets daily, as determined by physician. **Sup:** In bottles of 100 tablets.

Corrigendum: The correct spelling for Nepera Chemical Co.'s anti-tubercular drug (listed on page 58a, September issue) is PYRIZIDIN.

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Pruce, A. M.: J. Med. Ass. Georgia 40: 101, 1951



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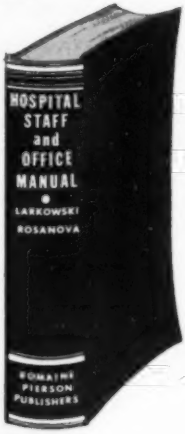
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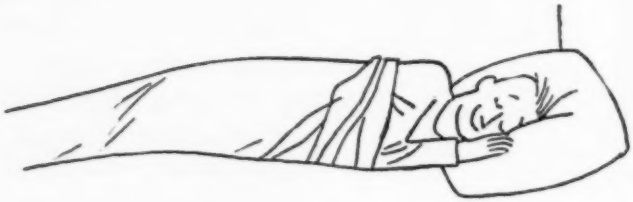
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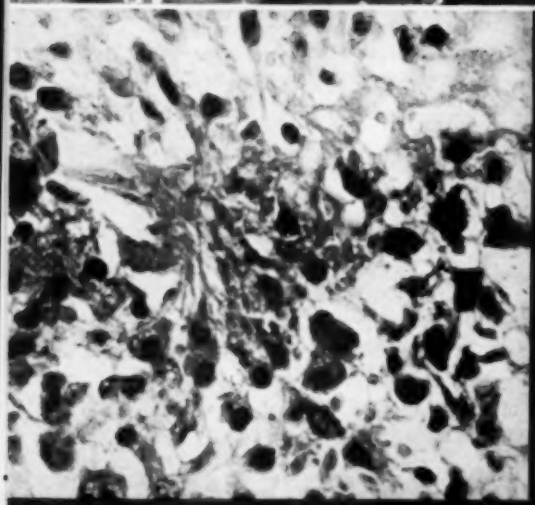
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1. Stone, A.: The Prevention of Conception, in Fishbein, M., and Burgess, E. W.: Successful Marriage, Garden City, N.Y., Doubleday & Company, 1947, pp. 279-80.
2. Stromme, W. B., and Rothnem, M. S.: Clinical Experience with a New Gel-Alone Method of Contraception, World Population Problems and Birth Control, Ann. New York Acad. Sc. 54:831 (May) 1952.
3. Hunter, G. W., Darner, C. B., and Gillam, J. S.: A Method of Contraception Without Diaphragm — A Two-Year Investigation, World Population Problems and Birth Control, Ann. New York Acad. Sc. 54:825 (May) 1952.
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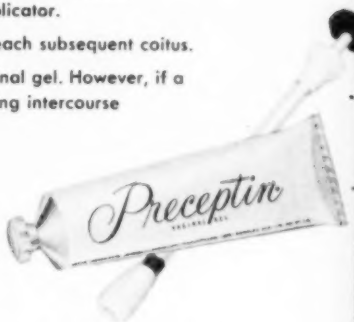
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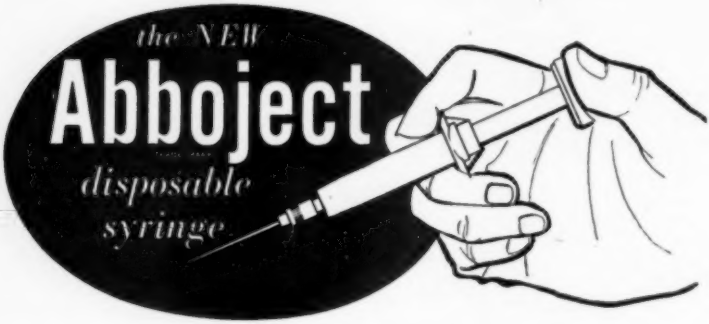
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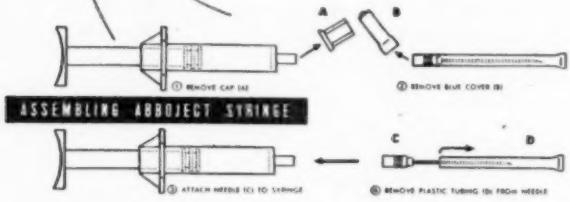
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Preventive Medicine in Anesthesia#

JOHN M. BROWN, M.D.*
Charleston, South Carolina

Historically speaking, the use of medical skill to prevent disease antedates rational therapeutics. This concept is recorded in the Holy Bible as certain inviolable laws of Leviticus,[1] and is demonstrated much later by the revolutionary teachings of Southwood Smith, Edwin Chadwick and others.[2] The anesthesiologist of today, primarily a physician, and secondarily an anesthetist, is trained to apply the modern concept of preventive medicine to anesthesia and obtains, as a direct result, a significant decrease in subsequent anesthesia morbidity and mortality.

In many places and under various circumstances, an anesthesiologist is not available, and the prevention of untoward difficulties during the operative period is placed into the hands of the attending surgeon or the family physician. These individuals, by understanding the problems encountered during anesthesia, and by meticulous attention to the patient during certain phases of the operative period, can prevent anesthesia complications as surely as the surgeon eliminates subsequent surgical complications by adhering to established surgical principles.

A comprehensive application of preventive medicine throughout anesthesia includes (1) the preoperative preparation for surgery, (2) the preanesthetic medication, (3) administration of the anesthetic drugs, and (4) the post-operative care of the patient.

Preoperative Preparation Preparation of a patient for surgery and anesthesia should begin at the time a diagnosis of pathology amenable to surgical treatment is established and the patient consents to operation. A comprehensive history will often elicit previous inhalation anesthesia difficulties or an obscure allergy to some regional anesthetic drug. A thorough physical examination will often reveal incipient pulmonary disease or cardiovascular incompetence. Laboratory examinations of the blood and urine may disclose an anemia or previously undetected diabetes mellitus.

If these routine procedures are performed early in the course of planning for a surgical operation, further investigations and treatment can be completed before hospitalization.

Poor oral hygiene, chronic sinusitis, and suppurative pulmonary disease require treatment prior to surgery. Anemia mark-

Presented at the PeeDee Medical Society meeting, Mullins, South Carolina, April 17, 1952.
*Associate Professor of Surgery (Anesthesiology), Medical College of South Carolina, Charleston, South Carolina.

edly alters the cardiovascular system[3] and must be corrected by transfusion or an appropriate medical regimen. Congestive heart failure reduces the status of a patient from a fair to a poor surgical risk. On the other hand, adequate digitalization vastly improves the status of such a patient as a surgical risk.

Various nutritional,[4] metabolic,[5] and fluid balance[6] disturbances are present in chronically ill, emaciated patients. Recent advances in parenteral nutrition provide new sources of supplementary feeding for these individuals, and, in many cases, constitute the only dietary avenues available throughout the surgical period.

An acute, upper respiratory tract infection doubles the incidence of postoperative pulmonary morbidity,[7] and ordinarily contraindicates elective surgery. Exacerbations of asthma and chronic pulmonary emphysema immediately before operation require that the contemplated surgical procedure be postponed.

Rapid preparation for operation is exemplified in the patient who develops pathology requiring immediate surgical intervention. Herein, whole blood transfusion and intravenous crystalloid and electrolyte therapy may be specifically indicated to quickly correct a deficiency before surgery.

Preparation of the stomach is one of the most important factors to consider before anesthesia. Regurgitation of gastric contents with aspiration produces many anesthesia deaths, and may occur during spinal anesthesia or thiopentobarbital anesthesia. Reverse peristaltic waves with profuse vomiting and sudden death are particularly likely to occur in patients with intestinal obstruction or head injury.

Nervous tension and accidental trauma greatly increase the emptying time of the stomach,[8] and a gastric tube may require hours instead of minutes to aspirate all gastric contents from the stomach under these circumstances. Beecher advocates induced vomiting with the stomach tube as the most satisfactory method of obtaining an empty stomach prior to the induction of anesthesia.[9]

Slow and difficult induction with an inhalation anesthetic agent increases the likelihood of vomiting. Volpitto and Benton advocate a rapid induction with Evipal sodium-decamethonium bromide and intubation of the trachea to obviate this difficulty during emergency anesthesia.[10]

Preoperative Medication Preoperative medication is indicated in all patients who undergo surgery, regardless of the type of anesthesia or the age of the individual. Excessive mucus formation, laryngospasm, overdosage of the anesthetic agent, cyanosis, or various cardiac arrhythmias may result from inadequate premedication.

The practice of ordering drugs "on call to the O. R." is dangerous, because maximum absorption frequently occurs after the induction of anesthesia and results in severe respiratory depression during anesthesia.

Preoperative medication includes a short-acting barbiturate the night before surgery, and again on the morning of surgery, if necessary for psychic sedation, hypnosis, or to prevent C. N. S. reactions from the subsequent use of a regional anesthetic drug. An opiate and belladonna derivative in a 25 to 1 ratio, when administered subcutaneously one hour before surgery, reduces the metabolic rate and reflex irritability, elevates the pain threshold, counteracts excessive mucus formation and abolishes the increased vagal tone produced by certain anesthetic agents.

Aminophyllin is employed as an integral part of the premedication to relax the bronchial musculature in asthmatic patients; papaverine and Paveril phosphate are employed to produce coronary vasodilation in the presence of coronary artery disease.

An obese patient is likely to require less premedication than a slender patient because the metabolic rate is likely to be

lower on an endocrinological basis. Pediatric patients and geriatric patients tolerate small dosages of the opiates as well as young, healthy adults if the reflex irritability and body surface of these individuals are taken into consideration when arriving at the dosages to be administered. Chronic alcoholics may be sedated with paraldehyde in relatively large dosage. Addicts and patients who are in shock are best premedicated by slow, symptomatic, intravenous injection of the drugs.

The wide range of preanesthetic drugs available permits the substitution or interchange of various drugs whenever a history of idiosyncracy to any specific drug is obtained from the patient.

The prophylactic administration of a peripheral vasoconstrictor immediately prior to spinal anesthesia makes this technique clinically acceptable in many cases. Repeated administration of a vasopressor such as ephedrine will often lead to tachyphylaxis or a "reversal" of its cardiovascular effectiveness. To prevent the occurrence of such phenomena, a pharmacologically dissimilar drug such as Neosynephrine (2-3 mg., intramuscularly) should be employed for any subsequent synergistic activity that becomes necessary during the course of anesthesia.

Anesthesia No ideal anesthetic agent or technique exists. Definitely adverse pharmacological actions and physiological alterations produced by the available anesthetic drugs and techniques of administration can be minimized or prevented, however, by employing established prophylactic measures.

The skillful use of pressure and packs will often control superficial bleeding encountered with inhalation anesthesia, and the use of small, subanesthetic quantities of ether vapor will often prevent ventricular premature contractions encountered during the administration of cyclopropane. The use of .2%—.4% thiopentobarbital as a basal narcosis, curare for relaxation, and nitrous oxide-oxygen with a flow rate of 2 liters of each per minute is pharmacologically sound. This technique tends to prevent the suboxygenation produced by thiopentobarbital or nitrous oxide-oxygen when either is employed alone for surgical anesthesia.

Nausea and vomiting frequently occur following the use of diethyl ether for anesthesia. Dramamine[11] and various other drugs have been employed to decrease the incidence of these undesirable side actions. Perhaps, prophylactic measures such as maintaining adequate oxygenation of the patient, preventing carbon dioxide excess, employing a uniform depth of anesthesia, and replacing fluids lost during surgery will produce results which are comparable to any specific drug therapy in these patients.

Difficulties may arise during anesthesia as a result of the technique of administering the anesthetic agent. Deep anesthesia with an open drop technique markedly reduces the arterial oxygen saturation. The administration of additional oxygen by a catheter underneath the mask is indicated under these circumstances. The semi-open drop technique should only be employed for short periods of time to prevent excessive accumulation of carbon dioxide, and should never be employed with divinyl ether because of the volatility and potency of this agent.

The semi-closed technique, during induction of anesthesia, necessitates frequent emptying of the re-breathing bag and a flow rate of approximately 5 liters of gases per minute with at least 20% oxygen in the delivered flow. This is the only technique that can be used to induce surgical anesthesia with nitrous oxide or ethylene without simultaneously suboxygenating the patient. The closed, carbon dioxide-absorption technique requires that the tidal air of the anesthetized patient never exceed the intergranular volume of the absorption canister to assure adequate absorption of carbon dioxide. The adult, carbon dioxide-absorption, circle filter

cannot safely be used for small children because of the great resistance to respiration. Asphyxia will rapidly develop under these circumstances unless adequate precautions are taken beforehand.

The use of flammable anesthetic agents such as diethyl ether, divinyl ether, ethylene, ethyl chloride, and cyclopropane in mixtures with air, oxygen, or nitrous oxide may be attended by a considerable risk of explosion unless adequate precautions are observed. Such a hazard may be reduced by educating all personnel to maintain a constant awareness of the possibility of an explosion and by the adoption of established scientific principles of explosion prevention in locations where these agents are employed. Recent directives outline a basic program for operating pavilions.[12]

Regional anesthesia employs many fundamentals of preventive medicine. The addition of epinephrine (1:50,000-1:200,000 concentration) to the anesthetic solution prevents rapid absorption of the drugs by local vasoconstriction of the area. Discoloration of an epinephrine solution indicates oxidation, and the bottle should always be discarded under these circumstances.

Sterile technique is inviolable during regional anesthesia, and careful needle technique resulting in perineural instead of intraneural injection is rewarded by a minimal number of postoperative neurological sequelae. The additional time and effort required to verify the concentration of a regional anesthetic drug, definitely establish its identity, or to prepare a fresh solution immediately before injection are rewarded by longer and more profound analgesia during surgery.

The position of a patient during surgery is important in the prevention of postoperative damage to the peripheral nerves. The arm should not be abducted beyond 90° on an armboard or brachial plexus damage may occur. The weight of a tired assistant on a leg supported by metal stirrups in the lithotomy position often produces common peroneal nerve damage which may be incorrectly attributed to subarachnoid anesthesia. The support of the arms at the sides of the table often determines whether or not ulnar nerve damage is produced by contact of the elbows with the table. All anesthetized patients should be gently moved and turned in a manner which prevents undue muscular stretching. Many postanesthetic back complaints are possible due to strains or sprains produced during movement under anesthesia.

Postoperative Care Postoperative recovery from surgery has changed dramatically within recent years. Months of slow, gradual improvement have been reduced to days of rapid convalescence. This has been partially accomplished by preventing many of the older familiar postoperative complications from appearing during the course of recovery.

Rapid emergence from anesthesia is desirable and constitutes an integral part of the program of early ambulation. A routine "stir-up" regimen should include orders to turn the patient every hour, and encourage deep breathing, coughing, and active movement of the legs every hour, when awake, for forty-eight hours following surgery. Patients who have had spinal anesthesia should remain in the horizontal position for at least six hours postoperatively to prevent an increase in hydrostatic pressure at the site of the dural puncture. Patients are allowed to sit in order to void.

Oxygen therapy is often of value in the immediate postoperative period. This may speed the return of vascular tone with early stabilization of the blood pressure, slow the pulse rate, produce a more rapid elimination of the anesthetic agent, lead to an earlier return of gastrointestinal peristaltic waves, or assure better oxygenation of a patient whose respirations are slightly depressed or whose airway becomes partially obstructed.

Recent investigations into the etiology, diagnosis, classification, and treatment of hypotension have resulted in more rational prophylactic measures.[13] The use of whole blood in hemorrhage, blood fractions and electrolytes in burns, the peripheral vasconstrictors in neurogenic hypotension, and intensive chemotherapy in the presence of overwhelming infection have reduced the incidence and severity of this complication.

The incidence of "postoperative pneumonia" has steadily decreased. The expectorant action of carbon dioxide-oxygen mixtures, the iodides, and water vapor therapy may be employed postoperatively to liquify tenacious bronchial secretions so that they can be more easily expectorated and do not remain in the lungs to produce atelectatic areas. Once atelectasis is established, however, intratracheal catheterization with suction or bronchoscopy becomes necessary to prevent subsequent consolidation of the area.

Recent experimental clarification of various pain mechanisms and pathways, and quantitative evaluation of the effectiveness of the analgesic drugs have contributed significantly to the control of postoperative pain[14]. Large dosages of the opiates only slightly increase the pain threshold above that obtained by a moderate dose. The hypnotic effect of the larger quantities can be obtained by the use of small amounts of barbiturates in conjunction with the analgesic agent. Demerol or Dromoran may be employed for the relief of postoperative pain where large amounts of morphine might produce smooth muscle spasm and actually intensify the pain.

The introduction of procaine in a solvent which allows precipitation of procaine crystals upon injection into the tissues (Efocaine) gives prolonged regional obtundation of pain with a significant decrease in the amount of narcotic required for pain relief.[15] In the geriatric patient, this method of controlling postoperative pain is of inestimable value because of the disorientation and lassitude likely to be produced by large dosages of the analgesic drugs.

Summary

Many complications of surgical anesthesia can be prevented if the attending surgeon or the family physician acquaints himself with the difficulties which are likely to be encountered in a particular patient who is given an anesthetic. The concept of preventive medicine when applied to the preoperative preparation for surgery, preanesthetic medication, administration of the anesthetic drugs, and the postoperative care of the patient will significantly decrease the subsequent anesthesia morbidity and mortality.

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Anticoagulants

This summarization attempts to cover the essential information on the subject and is designed as a time-saving refresher for the busy practitioner.

It has been long recognized that the clotting of blood is an important, protective, natural function in the absence of which even slight wounds might lead to serious consequences. When this clotting takes place, however, within the circulatory system itself, serious consequences, even death, may ensue. Recently, research on the therapeutic usefulness of a prolongation of the clotting time has opened new fields in medicine. The well known and unfortunate consequences of acute coronary thrombosis and the complicating effect of thrombosis on many chronic diseases have lead to extensive investigations into the effectiveness of anticoagulant agents in decreasing these life-endangering processes.

This work was greatly accelerated by discoveries involving two different compounds. One of these, heparin, was discovered by McLean[1] in Howell's laboratory in 1916, but was not purified sufficiently for clinical use until some twenty years later. In 1938, Solandt and Best[2] demonstrated that heparin was capable of preventing intravascular clotting in experimental animals. The second compound, Dicumarol, was the product of an amazing series of experiments by Link and his co-workers. In 1941, they reported the isolation and synthesis of this anticoagulant.[3]

Coagulation of the Blood According to the classical theory, the coagulation of blood takes place in the following manner:

Prothrombin + Calcium ion + Thromboplastin = Thrombin

Fibrinogen + Thrombin = Fibrin (clot)

One of the more recent theories proposes the interaction of six factors in the formation of the clot. Five of these, thromboplastinogen, calcium, prothrombin, the 'labile factor,' and fibrinogen are furnished by the plasma, while the disintegration of the platelets provides the sixth factor, an activator of thromboplastinogen. The mechanism may be pictured as follows forming an autocatalytic cycle (4).

Platelet disintegration → Thromboplastinogenase

Thromboplastinogenase + Thromboplastiogen → Thromboplastin

Thromboplastin + the Prothrombin complex (the 'labile factor', calcium, and prothrombin) → Thrombin

Thrombin + Fibrinogen → Fibrin

Thrombin + Platelets → further platelet disintegration

In order to prevent the cycle from continuing until all of the circulating blood has coagulated, certain safeguards exist: a) fibrin removes thrombin from the reacting system by adsorption; b) in the intact, unretracted clot, conversion of prothrombin is slow and is followed by continuous adsorption by the fibrin network; and, c) lysis of surface platelets liberates a powerful vasoconstrictor in addition to further thromboplastinogenase.

Quick[4] believes that the chief factors involved in the propagation of a thrombus are clot retraction and local sluggishness

of the circulation. As the clot retracts, thrombin-rich serum is expressed which, in the absence of an adequate blood flow, maintains a sufficiently high concentration of thrombin to cause fresh clotting on the surface of the thrombus and permits the process to continue. This method of propagation directed by the flow of blood in the direction of the blood stream explains why the thrombus is often found to be attached only at its point of origin (phlebothrombosis). It is probable that signs and symptoms such as pain, swelling, and tenderness indicate extensive attachment to the vessel wall (thrombophlebitis).

Heparin[1] is the natural, anticoagulant substance which takes part in the physiological function of maintaining the fluidity of the blood. It is found in all mammalian tissues. It is believed that the mast cells of Ehrlich secrete heparin[6] and it is found, therefore, in greatest concentration in liver and lungs. These organs, obtained from domesticated animals used for food by man, represent the source of supply for heparin. Chemically, it is a mucoitin polysulfuric acid, being a mixture of several sulfuric esters. The anticoagulant action is greater in preparations having a higher sulfur content.

Heparin interrupts coagulation by the following effects.[7]

1. It inhibits the agglutination of platelets, prevents the liberation of thromboplastin, and antagonizes liberated thromboplastin.
2. It prevents, with the aid of a plasma co-factor, the conversion of prothrobin to thrombin.
3. It forms, with serum albumin, a strong antithrombin.

Heparin is used as the sodium salt. Heparin Sodium U.S.P possesses not less than 100 U.S.P. Heparin units per mg. and it is available in solutions for intravenous use containing 10, 50, and 100 mg. per cc.[8] In this form, the action of heparin is very rapid, the anticoagulant effect developing within ten minutes. The effect is somewhat transient, however, due to the destruction of heparin by the enzyme heparinase present in the body fluids and due to the renal excretion of heparin. The effect of a single intravenous injection disappears in a matter of hours. In order to maintain therapeutic effectiveness, repeated injections of 50 mg. every four hours or 100 mg. every six hours must be made, or 200 mg. of the material may be added to 500 to 1000 cc. of an infusion solution such as normal saline or 5% glucose and administered by continuous intravenous drip at a rate of 20-25 drops per minute.

In order to reduce the number of injections required and to avoid the use of intravenous therapy, a solution of heparin in the Pitkin menstruum[9] was prepared. This permitted the intramuscular or deep subcutaneous injection of heparin and allowed for the slow release and the lasting effect of the substance. The original solutions gave pain at the site of injection but no other ill effects. Alteration of the pH through buffering resulted in a reduction of pain. Heparin preparations of the repository type (in a medium containing gelatin and glucose) are now available[10] and these eliminate the objections to intravenous therapy. In addition, repository heparin has been prepared with epinephrine and ephedrine as vasoconstrictors[11] which tend to prolong the effect still further. In the use of the latter, contraindications to the use of vasoconstrictors, such as in arterial thrombosis, should be borne in mind.

The repository forms are injected preferably into the deep subcutaneous tissues. A common site of injection is the anterior and lateral aspects of the thigh. They are never injected intravenously. The contents of the ampul should be liquefied by holding it under hot tap water. With this material, effective, elevated coagulation times are maintained for 24 to 48 hours following a single injection of 400 mg. of heparin sodium. If so desired, 200 mg. of the plain form and 200 mg. of heparin with

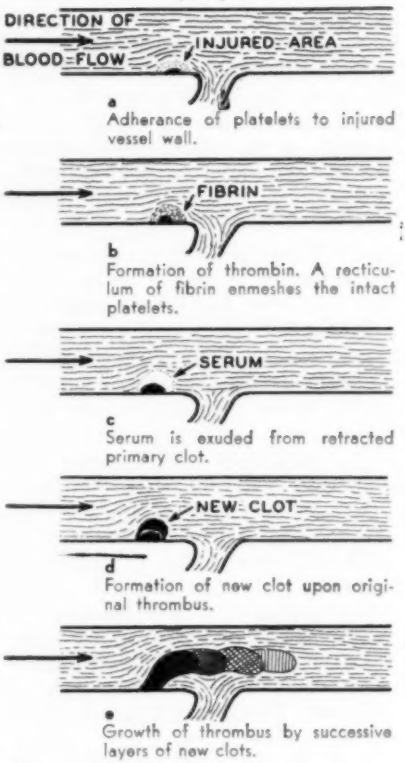
vasoconstrictors may be given. This is followed by additional injections of 200 mg. every 12-24 hours as indicated. If an immediate rise in coagulation time is necessary, 50 mg. of aqueous heparin may be given intravenously at the time of the first repository injection. The action of heparin may be prolonged also by the oral administration of carinamide, which delays the renal excretion of heparin[12] or by dicumarol which increases sensitivity to heparin.[13] The dosage of heparin is adjusted so as to maintain the venous clotting time between 30 and 60 minutes, depending upon the method used for the determination, or approximately 3 to 4 times that which is normal for the patient.

The successful use of heparin orally has been accomplished experimentally.[45] In ten cases therapeutic levels were obtained in one half hour and were maintained for four hours. This was accomplished by the use of wafers or pellets which were placed in the sublingual pouch where they rapidly disintegrated and absorption was usually complete within ten minutes. This route of administration has unquestioned advantages. The authors state that oral administration will have particular value to the soldier in the field.

While such occasions have been found to be rare, the possible necessity of retarding the effect of the anticoagulant or of bringing the coagulation time rapidly back to normal has received attention. Ice bags retard and prolonged local refrigeration completely stops the effect of an injection of the repository form of heparin. The effect of heparin can also be counteracted by transfusions of 250-500 cc. of fresh whole blood and by the use of the heparin antagonists, Protamine Sulfate[14] and toluidine blue. Protamine Sulfate, 50 mg., is given by slow intravenous injection with or without dilution with normal saline. The heparin-protamine ratio is approximately 1:1.

Heparin does not affect osmotic pressure, the red or white blood cells, hematocrit values, or antigens. It is compatible with sulfonamides and penicillin.

Fig. 1
Thrombus formation (diagrammatic after Quick).



The use of heparin is contraindicated following recent surgical operations on the brain and spinal cord, in obstructive jaundice and extensive liver disease, and in the presence of a hemorrhagic tendency, such as in ascorbic acid deficiency, hemophilia, and in purpura hemorrhagica. It should be used only with great caution following operations on the biliary tract. Should spontaneous nosebleed or other bleeding occur, heparin should be discontinued.

Dicumarol [8, 15] [Bishydroxycoumarin U.S.P.; 3, 3'-methylenebis (4-hydroxycoumarin)] is the potent, orally

effective, anticoagulant originally isolated from spoiled sweet clover[3] and now prepared synthetically. It interferes with coagulation by decreasing the prothrombin concentration of the blood. Following administration of the drug, there is a latent period of 24-48 hours. The prothrombin time slowly increases and it remains elevated for 2-10 days after cessation of therapy.

Since increase in blood clotting time is not proportional to reduction in prothrombin concentration, the results of dicumarol therapy must be carefully followed by the determination of prothrombin time or activity. Therapeutically it is desired to obtain and maintain a prothrombin activity of about 25% of normal. This is usually brought about by giving 200-300 mg. as the initial dose, depending upon the size and condition of the patient, and following with 100-200 mg. on those days when the prothrombin activity rises to 25% or above. It should be borne in mind that the effects of dicumarol are cumulative and that daily determinations of prothrombin time should be made. No dose of dicumarol should be given until such a test has been performed. If prothrombin activity is low initially, dicumarol must be given with caution and in smaller dosage.

Reduction of prothrombin activity to less than 10% is regarded as dangerous. In such cases and in any case in which it is desired to raise prothrombin activity, transfusions of fresh whole compatible blood, fresh citrated blood, or fresh plasma should be given. In addition, large doses of vitamin K preparations[16] equivalent to 40 mg. of menadione may be injected. The maximal effect of the latter is not attained for approximately eight hours. It is obvious, therefore, that dicumarol can be given only to patients in hospitals in which facilities for proper control and management exist.

The hemorrhagic tendency from the use of dicumarol may be manifested by hematuria, by petechiae in the skin, by hemorrhage into or from a wound or ulcerating lesion, or by petechial and purpuric hemorrhages throughout the body. Patients should be examined daily for evidence of these complications and the urine tested for hematuria. If hemorrhage into the bowel is suspect, the stool should be examined.

Dicumarol, in therapeutic doses, does not seem to affect the erythrocytes, leukocytes, or blood platelets. It does not appear to affect the values for blood sugar, blood non-protein nitrogen, serum calcium, bilirubin or the hematocrit. While it does not seem to have any effect on liver or renal function, impaired renal or liver function will accentuate the effect of dicumarol.

The use of dicumarol is contraindicated in the presence of ulcerating or granulomatous lesions, in subacute bacterial endocarditis, and in patients being submitted to continuous tube drainage of the stomach or small intestine. It should be used with special caution in patients seriously ill, debilitated or cachectic; in the presence of impaired liver or renal function, jaundice, hepatic cirrhosis, or enlargement of the liver; in menstruation, menorrhagia, or metrorrhagia; in febrile patients; in certain poor nutritional states; and, following operation on the brain or spinal cord. Blood dyscrasias, hemorrhagic tendencies, and definite hypertension also requires that special precautions be observed if the drug is to be used at all.

Certain drugs, such as digitalis, theobromine and theophylline, are believed to possess a thrombogenic property, while salicylates and quinine have a dicumarol effect.[17]

Combined Heparin-Dicumarol Administration overcomes one of the disadvantages of dicumarol therapy. It makes possible an immediate effect, that of heparin, on the coagulation time during the induction period of dicumarol. The patient may be given heparin sodium, 100-125 mg., intravenously and dicumarol 200-300 mg., orally. Heparin is continued at

the level of 50-100 mg. every four hours for three additional doses. The last dose may be raised to 100-125 mg. In this manner, 300-450 mg. of heparin are given daily until the dicumarol becomes effective. Alternatively, 400 mg. of repository heparin, half of which may be combined with vasoconstrictors, if indicated, may be injected into the deep subcutaneous tissues and again 200-300 mg. of dicumarol is given orally. In any case, the normal prothrombin time should be determined before the

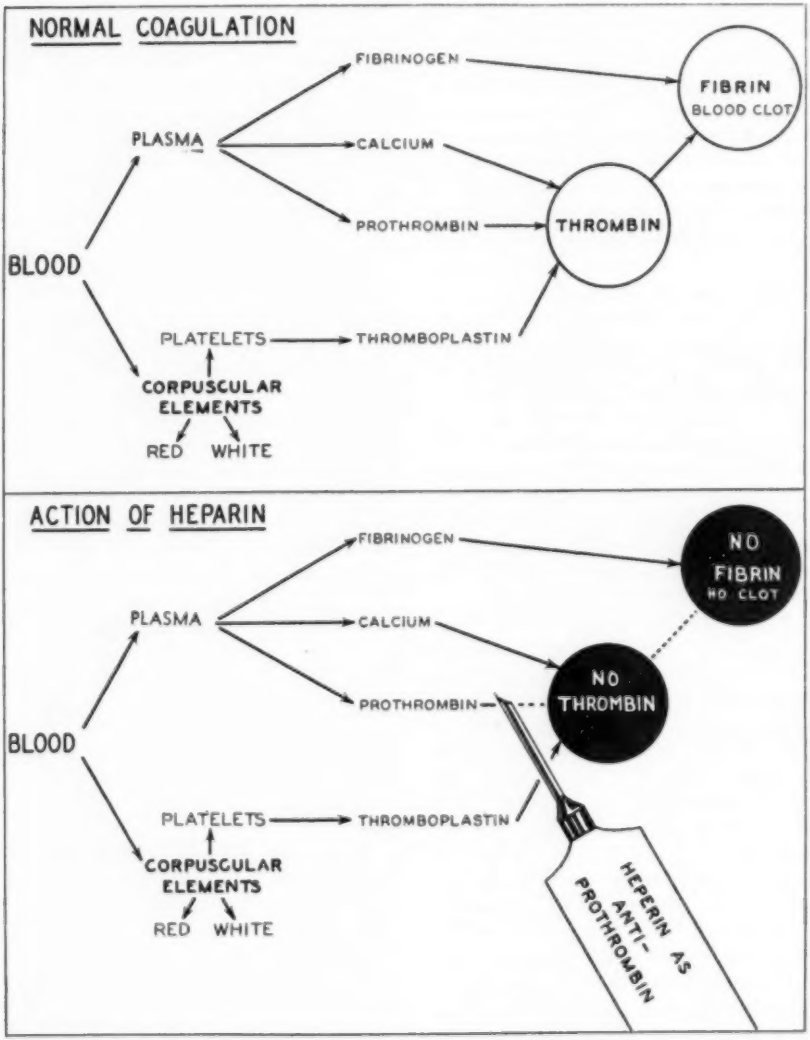


Fig. 2. Chart showing mechanism of blood clotting and of the anticoagulant action of heparin.

start of therapy. It should be remembered also, that blood obtained too soon after heparin administration may give a false prothombin time because of the anticoagulant effect of the heparin present.

Control of Anticoagulant Therapy Anticoagulant therapy cannot be carried out unless suitable means for control exist. Since the therapeutic effectiveness of heparin is dependent upon and is measured by an increase in the blood clotting time, it is essential that regular determinations of this function be made. While the capillary tube method is favored in some quarters[18] because of the ease and rapidity with which it can be carried out at the bedside, many investigators prefer the Lee-White method,[19] using a one or three tube technique, since the blood is drawn from a vein in the latter method and it is not mixed with tissue fluid which influences blood clotting time. Loewe[20] recommends a modification of the Lee-White method in which the end point is read in the red cell layer. This is possible because the cells settle rapidly in well heparinized blood, before clot formation. It will be noticed that a plasma fibrin clot will form before solidification occurs in the red cell layer. Since formation and extension of the thrombotic process depends upon the cohesiveness of the red blood cells, the end point is read when the red cells clot and not at the time the fibrin clot is formed in the plasma. In blood which is not well heparinized, the end point is read when the blood fails to run down the side of the tube during gentle tilting.

After the normal coagulation time has been determined and therapy instituted with repository heparin, coagulation times should be determined every 12 hours for the first 48 hours, then every 24 hours or as frequently as deemed necessary. In the case of intravenous heparin administration coagulation times must be determined more frequently, particularly during the initial period. de Takats[44] recommends the use of a heparin tolerance test before the institution of therapy.

For proper control during treatment with dicumarol, which affects prothrombin production, it is necessary to study quantitatively the prothrombin concentration in the plasma. This is necessary, rather than a clotting time determination, because dicumarol does not affect the clotting time of whole blood until prothrombin has fallen to less than 30% of normal. Prothrombin determinations are made by a method originated by Quick.[21, 22] In this method thromboplastin (prepared from rabbits brains) in excess is added to oxalated plasma and then recalcified. The time in seconds required for fibrin to form is recorded as the prothrombin time. With this method normal prothrombin time may be from 12 to 14 seconds. Samples requiring a considerably longer time are thought to be definitely lacking in prothrombin. Since there may be considerable variation in the thromboplastin preparations, it is customary to prepare prothrombin activity curves for each lot of thromboplastin used. These curves are prepared with observations made on different dilutions of 'normal' plasma. Results obtained in test samples are then read in terms of percentage of prothrombin activity. Variations of the original method are in use.[23, 24] Thromboplastin preparations may be prepared from lungs also. Brambel and Loker[25] found that the 12.5% plasma preparation made by dilution with isotonic sodium chloride was the most sensitive dilution with reference to indicating an increase in plasma prothrombin time. At this dilution, they found the average prothrombin clotting time, based upon 75 healthy persons chosen at random, to be 95 seconds, with figures from 85 to 105 seconds considered to be 'normal'. Other investigators have reported a value of 40 seconds for this dilution.

Prothrombin tests should be performed only by experienced workers. Because of variations in method, technique, and

thromboplastin preparations, all reports should give percentage of prothrombin activity as well as time in seconds. Percentage of prothrombin activity will usually be the more accurate guide to proper dosage with dicumarol.

Clinical Applications Few therapeutic agents have found the wide range of therapeutic usefulness which is characteristic of the anticoagulants. Their effectiveness is well established in the treatment of all forms of venous and arterial thrombo-embolic disease and in the prevention of thrombo-embolic complications. The importance of anticoagulants can be appreciated when one considers the fact that hemorrhage causes many fewer deaths than does intravascular coagulation of blood.[26]

In these conditions the factors of stasis and of endothelial injury have been emphasized. In addition one should consider carefully the factor of postoperative or post-traumatic hypercoagulability. Quick[7] has noted that coagulation of the blood in vivo becomes enhanced following trauma. de Takats[18, 44] has devised a heparin tolerance test by means of which it is possible to detect persons whose blood has an increased tendency to coagulate. Shapiro and his coworkers have shown that estimations of the clotting time of prothrombin in dilute plasma likewise give an index to post-traumatic coagulative tendencies.

de Takats[44] believes that when the diagnosis of thrombosis or embolism has been made, whether in the cerebral, retinal, coronary, pulmonary or peripheral arteries or veins, intensive anticoagulant therapy must be instituted for three reasons:

1. In order that propagation of the thrombosis may be stopped:
2. In order that early lysis of the clot with canalization of the vessel may be observed; and,
3. In order that exudation of plasma through anoxic capillaries which is followed by plasma clotting in the tissues can be retarded or inhibited.

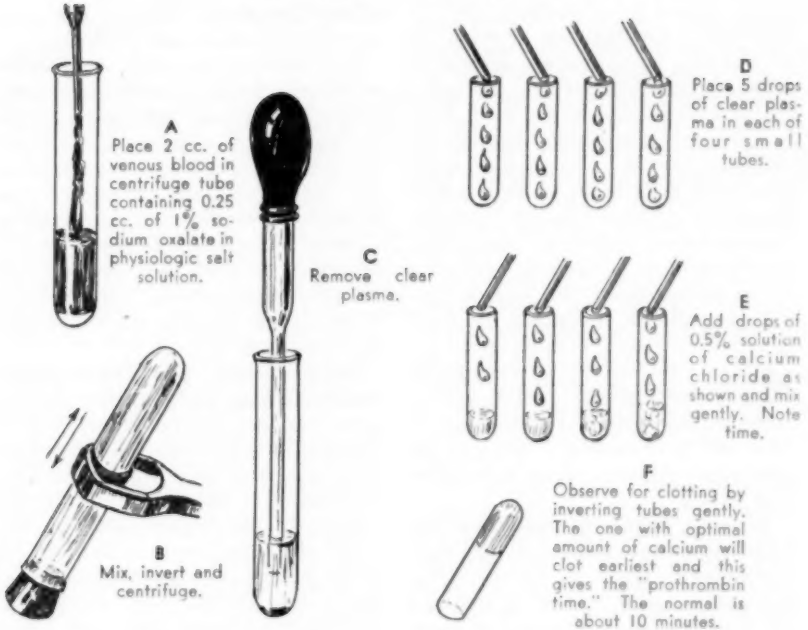
Allen[26] has outlined some of the more important indications for anticoagulant therapy as follows:

1) After non-fatal pulmonary embolism to prevent further embolism which may be fatal
2) In thrombophlebitis and phlebothrombosis to prevent further venous thrombosis and pulmonary embolism and to lessen the possibilities of resultant chronic venous insufficiency (edema, varices, ulcers, and indurative cellulitis)
3) In sudden arterial occlusion (embolism and thrombosis) to prevent arterial thrombosis which results from ischemia of the intima (distal to the area of occlusion) and to prevent thrombosis of an artery at the site of embolectomy if a surgeon removes the embolus
4) To avoid thrombosis in cases of traumatic injury to the blood vessels
5) As prophylaxis against postoperative venous thrombosis in cases of previous thrombosis or embolism, because of the increased probability of further venous thrombosis or embolism
6) After abdominal hysterectomy, appendectomy, herniorrhaphy and prophylactically after other operations.

Non-Fatal Pulmonary Embolism Two hundred ninety two cases of pulmonary embolism were treated with anticoagulant therapy (dicumarol). Subsequent venous thrombosis or pulmonary embolism occurred in only three cases whereas occurence in 127 was expected. One death occurred (after the prothrombin time had returned to normal) due to fatal pulmonary embolism compared with 53 expected.[26]

Swedish investigators using heparin in 769 cases and dicumarol in 131 cases of pulmonary embolism, found that less than 1% of those cases receiving anticoagu-

Fig. 3. Test for prothrombin time (Howell).



lants died because 16% of the control cases died (in 27).

Thrombophlebitis and Phlebothrombosis Bauer[28] treated 209 cases of acute thrombosis of the deep veins of the leg with heparin. The mortality rate was reduced to one tenth of that expected. The stay in bed was reduced from about 40 days to less than 5 days and incapacitating after effects apparently did not occur in a majority of the cases.

Favorable results have been obtained in the treatment of superficial phlebitis, deep phlebitis, and superficial and deep phlebitis, 47 cases in all, with dicumarol.[29] Diminution or disappearance of pain or tenderness over the affected area were used as criteria for remission. The drug was given for at least ten days. Many of the patients were postoperative and 19 were postpartum obstetrical cases. Anticoagulant therapy was found to be superior to other forms of therapy because of the diminution in the length of time of treatment and the lack of complications referable to dicumarol or to the phlebitis. Since pain is markedly reduced, the amount of sedation needed is markedly diminished.

Coronary Thrombosis and Myocardial Infarction In a cooperative study, observations were made on 800 cases of coronary thrombosis with myocardial infarction.[30] Of these, 432 received combined heparin-dicumarol anticoagulant therapy; the remainder were 'controls' and received conventional treatment. There were one-third fewer deaths in the treated group than in the control group. The authors state that anticoagulant therapy, if not used sooner should be begun as late as the second or third week and should be

continued for at least four weeks. Treated patients showed less development of thrombo-embolic complications. Failure of dicumarol in some cases was believed to be due to the fact that the prothromin time was not adequately prolonged. Total hemorrhagic manifestations not due to anticoagulants in the treated group approached those found in the untreated group. An additional seven cases per hundred showed hemorrhagic effects which were believed to be due to or aggravated by the anticoagulants. The greatest benefit in the reduction of mortality was found in patients 60 years of age or older.

In myocardial infarction anticoagulant therapy is of particular interest because of the frequent occurrence of mural thrombosis over a myocardial infarct and the subsequent occurrence of severe and often fatal emboli.[31]

Trauma, Frostbite and Gangrene It has already been mentioned that following trauma, surgical or accidental, the coagulability of the blood is enhanced and that this can be expressed in terms of an increased activity of prothrombin and resistance to heparin. In trauma with gangrene not only are conditions manifest which favor thrombus formation but also there is marked swelling which interferes with normal circulation and oxygenation of the tissues. Gangrene may readily develop in the extremities four to seven days after trauma that has resulted in lacerations and severe crushing injuries.

Brambel and LokYer[32] found that postoperative amputation was unnecessary in six cases of severe accidental trauma of the extremities in which heparin-dicumarol therapy was instituted immediately following surgical repair. Recovery was uneventful and healing by first intention occurred. No bleeding occurred as a result of the administration of the hemorrhagic compound. Three cases of diabetic gangrene and one of arteriosclerotic gangrene were benefited by the use of dicumarol, in addition to conventional treatment, to the extent that the amount of surgical intervention required was much less than expected in such cases.

The frequent occurrence of frostbite in the armed forces stimulated research which demonstrated that antocoagulants prevented the development of thrombosis and gangrene. The most recent report on this subject[33] covers 14 civilian cases treated with heparin and discumarol in addition to standard treatment for the prevention of shock and infection. Only one patient required local amputation of a finger, and the duration of hospitalization was appreciably reduced.

Prophylactic and Therapeutic Use Following Surgery Dicumarol administerred prophylactically to a group of 102 surgical patients prevented thrombotic phenomena and there was no postoperative bleeding.[34] The group included cases of hernioplasty, hysterectomy, appendectomy, cholecystectomy, laparotomy and other miscellaneous cases. Since statistics have shown that thrombosis and pulmonary embolism do not begin until aproximately the sixth or seventh postoperative day, administration of the drug was started on the third or fourth day. The danger of postoperative pulmonary embolism diminishes considerably after the fourteenth day.

After 2591 general surgical and obstetrical procedures, the typical cases of venous thrombosis and pulmonary embolism that occurred were also treated with anticoagulants.[34] Dicumarol, carefully administered, prevented extension of the thrombus. The thrombophlebitis was resolved and none of the pulmonary emboli caused fatal results. In acute cases of pulmonary embolism, heparin was administered by vein and dicumarol by mouth at the same time.

Crafoord and Jorpes[35] found no thrombo-embolic phenombena in 325 patients treated postoperatively with heparin although such complications occurred in 9% of a control series of 1,111 similar cases.

In 280 cases of postoperative throm-



Fig. 4. Coagulation time by capillary tube method. Clotting occurs when strands of fibrin stretch between the pieces of pinched off tubing. Normal time is 3 to 8 minutes.

bophlebitis receiving anticoagulant therapy (dicumarol) subsequent occurrence of venous thrombosis or pulmonary embolism was reduced from an expected 68 cases to 8 cases. No cases of fatal pulmonary embolism occurred although 16 were predicted. In 716 cases of abdominal hysterectomy, similar benefit from the use of dicumarol was observed.[26]

Leissner used heparin prophylactically in 50 obstetrical cases in which he considered that there was relatively great risk of thrombosis. Thrombotic complications occurred in only two patients[36].

Miscellaneous Additional conditions reportedly benefited by the use of anticoagulants include cavernous sinus thrombosis,[37] thrombophlebitis migrans,[27, 38] thromboangiitis obliterans,[39] and rheumatic fever with embolism.[27]

Experimental Use Wylie and his coworkers report the experimental use of a method for the continuous intra-arterial infusion of heparin during surgery on blood vessels. This permits adequate anticoagulant levels locally without any systemic effect.[40]

Preliminary studies on the use of heparin in burns indicate that reparative processes are more efficient and the healing time is shortened.[41] In dogs with experimentally-induced massive burns (approximentally 43% of the surface area), heparinized animals survived twice as long as controls. None of the animals received supportive treatment.[42]

Heparin in Transfusion Heparin may be used to replace or enhance the action of sodium citrate in blood transfusion work. This may be carried out by one of two methods. In the first method, the donor is given aqueous heparin, usually 50-100 mg. Blood is drawn when the coagulation time has been markedly increased. The transfusion should be completed within the clotting time of the donor's blood. This procedure enables the physician to give whole blood free from any substance not normally present and eliminates clotting in the vein or needle.

In the second method, 50 cc. of sterile normal saline and 20 mg. of heparin sodium are introduced into a sterile flask for each 100 cc. of blood to be drawn. The transfusion should be completed within an hour. Heparinized blood cannot be banked as heparin is destroyed within a few hours.

Wiener and Wexler[43] have used aqueous heparin, 1000 units (1 mg.) divided into two portions, to aid in the performing of a complete exchange transfusion in newborn infants, a procedure which may be indicated in the severe cases of icterus gravis.

Conclusion

The ideal anticoagulant has been said[29] to be one which (a) lacks harmful side effects regardless of period of use, (b) gives a predictable effect for a specified amount of drug, (c) may be promptly controlled, if necessary, (d) has an effect which may be tested in a simple, rapid manner, (e) is effectvie on oral administration, and, (f) is inexpensive. Obviously, all of these conditions cannot be met at the present time. Nevertheless, the physician has available two potent drugs, which, if judiciously used with proper control, can do much in the alleviation of pain and suffering and can save many lives, formerly doomed prematurely due to thrombo-embolic phenomena.

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The International Academy of Proctology 1952 Award Contest

The International Academy of Proctology takes pleasure in announcing its Annual Cash Prize and Certificate of Merit Award Contest for 1952-1953. The best unpublished contribution on Proctology or allied subjects will be awarded $100 and a Certificate of Merit. Certificates will be awarded also to physicians whose entries are deemed of unusual merit.

The competition is open to all physicians in all countries, whether or not affiliated with the International Academy of Proctology. The winning contributions will be selected by a board of impartial judges, and all decisions are final.

The formal award of the First Prize, and a presentation of other Certificates, will be made at the Annual Convention Dinner Dance of the International Academy of Proctology in May of 1953.

The International Academy of Proctology reserves the exclusive right to publish all contributions in its official publication, The American Journal of Proctology and Gastroenterology.

All entries are limited to 5,000 words, must be typewritten in English, and submitted in five copies. All entries must be received no later than the first day of April, 1953. Entries should be addressed to the International Academy of Proctology, 43-55 Kissena Boulevard, Flushing 55, New York.

Acute Appendicitis†

Diagnosis and Treatment

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Since acute appendicitis still accounts for numerous deaths each year, a revival of interest and a renewal of methods of attack surely seem warranted. The statement "only an appendix" is indeed a dangerous one. Certain specific ideas concerning the diagnosis and treatment of acute appendicitis have been formulated after studying this condition for the past seventeen years.

In 1886 appendicitis got its name from Reginald Heber Fitz of Harvard. His description is considered one of the classics in medical literature. It is odd, however, that the condition was not discovered or described in the literature until such a late date. Anatomically the appendix was described in the sixteenth century; pathologically it was recognized in the eighteenth century; clinically it belongs to the nineteenth century; and therapeutically it is the challenge of the twentieth century.

Pathologic Physiology In discussing inflammation and infection the late Richard Jaffe stated: "There is no infection without stasis." Thus, if a gallbladder can empty itself there will be no cholecystitis, if a sinus drains itself there will be no sinusitis, and if an appendix evacuates itself there will be no appendicitis.

Micro-organisms always are present, but as long as they are kept in motion they cannot increase in number and so do not gain a foothold in the tissues; thus no inflammatory response results. Fecaliths, kinks, bands, spasms, mucosal folds, or foreign bodies might act as the obstructing factor and permit the bacteria to multiply. How far this inflammatory response will progress cannot be foretold. It depends upon the completeness of the obstruction, the virulence of the micro-organism and the resistance of the host.

History and Symptoms Certain types of people are predisposed to certain types of diseases. We know that the characteristic type for acute appendicitis is the YOUNG ADULT MALE in his teens and second or third decades. There is no dogma in medicine, and although this disease may occur at any age, it becomes infrequent after the age of forty.

Any diffuse epigastric distress which localizes to the right lower quadrant within the first 24 to 48 hours is acute appendicitis until proved otherwise. Unfortunately, however, our patient does not use this terminology, but relates the same story in a different way. His terms for diffuse epigastric distress are: "belly-ache," "spoiled stomach," "cramps," or "gas."

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His usual remark is: "Something I ate gave me a bellyache." He ofttimes heeds the advice of a well-meaning friend who suggests a cathartic, and then some 24 hours later becomes concerned about a "sore spot" in the lower right side of his abdomen. It is at this time that he will usually consult the doctor.

The TWO QUESTION TEST suggests the diagnosis in well over 70 per cent of cases of acute appendicitis. Question number one: "Where was your pain when it started?" To this the patient usually points to his entire abdomen. Question number two: "Where does it hurt you now?" To this interrogation the patient usually points to the region of McBurney's point. This is one of the simplest, most efficacious and rapid methods of diagnosing a case of acute appendicitis.

Unfortunately nausea and vomiting have been taught as being frequent symptoms. This is not true. The majority of patients neither vomit nor complain of nausea; almost all, however, have anorexia. Anorexia, nausea and vomiting are really three degrees of one symptom being dependent upon the degree of distention in the appendix. Vomiting is associated with a markedly distended appendix. Since almost all acute appendices are associated with such distention these patients should complain of anorexia. It is indeed a rarity to find a patient suffering with acute appendicitis stating that he is hungry.

Physical Examination A high initial fever strongly suggests some other condition but not acute appendicitis. The fever is usually of low grade in early appendicitis but as the disease progresses, especially after the first 24 to 48 hours, the fever begins to rise as the peritoneal cavity becomes soiled. One, therefore, should not wait for the fever to develop since it indicates a complication rather than acute appendicitis per se. This rule does not apply to children since they will develop a hyperpyrexia on the slightest provocation. The pulse is seldom of great diagnostic value. The so-called diagnostic ratio should be kept in mind, namely, that for every degree rise in temperature there is a ten beat increase in pulse. The respiratory rate is normal or often proportional to the fever; as peritoneal soiling progresses it increases. The patient with an uncomplicated acute appendicitis usually does not appear to be seriously ill; in fact his appearance may be quite misleading as he walks into the doctor's office. Rarely have I found these patients lying in bed with the right knee raised as is described so routinely in many textbooks.

The tremendous number of specific signs which have been associated with the diagnosis of this condition are not only exhaustive but exhausting; they have little or no practical value. To describe Bastedo's sign, Klemm's sign, Walkowitsch's sign, Reder's sign, Aaron's sign, Morris' sign and many others too numerous to mention is only a display of academic muscle. Only those few signs, or tests, which are of practical value will be evaluated.

McBurney's Point This is a point of maximum tenderness as determined by the pressure of one finger. It is located in the following way: a line is drawn between the right anterior superior iliac spine and the umbilicus; this line is trisected. McBurney's point will be found where the lateral and middle thirds meet. A state of confusion seems to exist as to whether this point remains fixed regardless of the position of the appendix. Although it has been stated that the nerve endings of the eleventh and twelfth dorsal segments are reflexely irritated by an inflamed appendix, practical experience suggests that the true point of tenderness is dependent upon the position of the appendix and not the fixed nerves.

Right Rectus Rigidity Increased tonus of the abdominal muscle, or so-called rectus rigidity, is not a sign of acute appendicitis, but rather a sign of peritonitis. We

know that it is usually quite impossible to contract one rectus muscle without contracting the other. Why then do we refer to the sign as *right* rectus rigidity when both recti contract? To correctly test for this sign the examiner must place both hands on the abdomen of the patient, one on each rectus muscle. With gentle pressure he determines whether or not one rectus is rigid and the other relaxed. If such a condition exists and only one rectus muscle is found to be rigid, then this suggests a mass underlying that rigid rectus. Such masses in the case of acute appendicitis would be either a localizing inflammatory appendical mass made up of appendix, terminal ileum and omentum, or an appendical abscess. When both recti are rigid it denotes a muscular defense in response to an underlying peritonitis. Should such a rectus suddenly be released the patient will wince because of so-called rebound tenderness (Blumberg's sign).

Obturator Internus Sign This sigr locates an acutely inflamed appendix but does not diagnose it. It is performed by bending the knee and internally rotating the flexed thigh. This maneuver places the obturator internus muscle through its full range of movements and will cause hypogastric pain if an acutely inflamed appendix overlies its fascia. Pelvic inflammatory disease as well as an acute pelvic appendix can produce a positive obturator sign.

Iliopsoas Sign This is not a diagnostic sign for acute appendicitis, but rather one which locates an inflamed appendix lying retrocecally and involving the fascia which covers the psoas muscle. It is conducted in the following way: the patient is placed on his left side and the right thigh is fully extended. If pain over the appendical area is produced by this maneuver the test is considered positive.

Rovsing's Sign This sign is considered positive when pain over McBurney's point is produced by exerting pressure over the descending colon. Supposedly it is due to a retrograde inflation of the cecum when colonic gas is forced from left to right in the presence of an inflamed appendix.

No physical examination is considered complete without a rectal or so-called bidigital examination. The latter is done, whenever possible, by placing the index finger in the vagina and the middle finger in the rectum. This will readily identify the cervix or adnexal pathology, a bulging cul-de-sac of Douglas, or fecal masses. Thus, greater orientation is obtained than is possible with a rectal or bimanual examination.

Laboratory Data The laboratory data is a helpful adjunct in the diagnosis of acute appendicitis; however, it does not replace a carefully taken history and a well conducted physical examination. The differential blood count is at times more helpful than the total blood count; however, both of these are done routinely. Urinalysis is also a necessary procedure but may be misleading. If the inflamed appendix is located near or on the bladder, the ureter or the kidney, a few red cells may appear in the urine thus masking the picture. On the other hand, a rather large ureteral calculus may plug the ureter so thoroughly that no pus or blood can pass into the bladder and again the clinician is misled. Of late we have utilized the flat roentgenogram of the abdomen in those cases where the diagnosis is somewhat uncertain. Much work has been published recently regarding the isolation of fecaliths in the appendix as shown on stereoscopic views. This is helpful both in the direct and the differential diagnosis and should be kept in mind.

Differential Diagnosis Although a tremendous number of diseases have been confused with acute appendicitis, for practical purposes, one must be thoroughly conversant with the usual conditions which cause the greatest diagnostic difficulties. The vast majority of our errors are found in the following five conditions: perforated peptic ulcer, acute gallbladder, renal colics, salpingitis and acute pancreatitis.

Perforated peptic ulcer is almost always found in males. A history is elicited of a sudden dramatic attack of pain which doubled the patient up, forcing him to stop whatever he happened to be doing. Abdominal auscultation usually reveals a silent abdomen, and the roentgen demonstration of a spontaneous pneumoperitoneum is quite diagnostic. Tenderness is quite diffuse, the abdomen is board-like, the patient looks more ill, and shock may be present. The pin-point perforation the forme fruste ulcer will present a misleading picture.

Acute gallbladder disease is more common after the age of forty. The gallbladder patient is usually the fair, fat and forty type of individual with a history of selective dyspepsia and/or a previous similar attack. The pain is usually above the umbilicus and the tenderness is localized to the right upper quadrant of the abdomen. At times Head's zones of hyperesthesia will reveal the hyperesthetic area above the umbilicus and to the right, whereas such an area is found below the umbicilicus in acute apendicitis. The pain is much more severe in acute cholecystitis and the patient usually requires sedation (this is most unusual in acute appendicitis).

Renal colics may be caused by stones, uratic debris, microscopic thrombi or a dropped kidney with a Dietl's crisis. The pain is usually in the loin, radiates along the course of the ureter, and then into the inner aspect of the thigh or the genitalia.

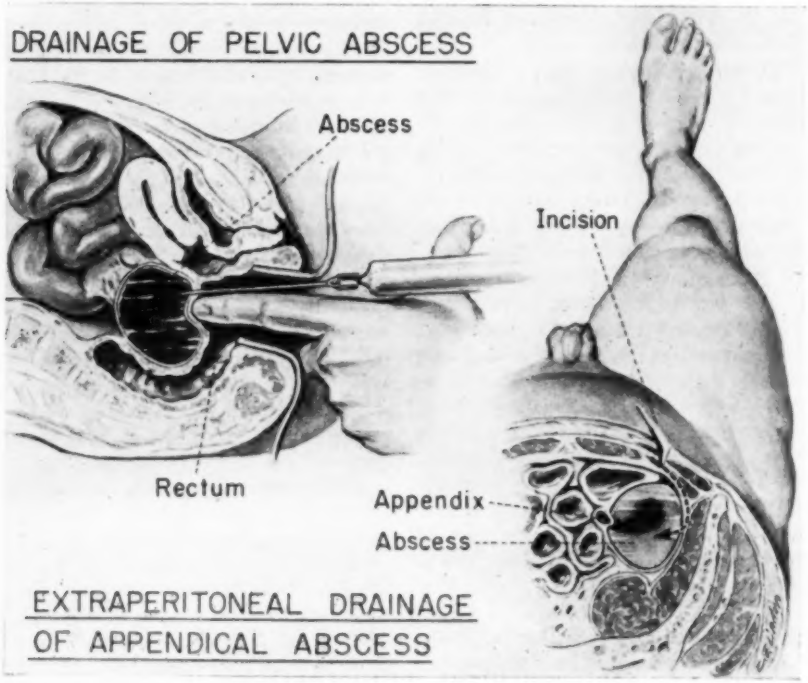


Fig. 1. Appendical abscesses may form either in the cul-de-sac of Douglas or in the right lower abdominal quadrant. The location and drainage of these abscesses are herein described.

A bradycardia is very characteristic of renal or ureteral colic. Tenderness over the kidney area is usually present. Red blood cells in the urine are most suggestive. In cases where great doubt exists emergency intravenous pyelography may provide the final answer.

Salpingitis usually occurs immediately before, during or after the menstrual period. It is extremely rare after the menopause. Tenderness is usually bilateral and over the region of the symphysis; on bimanual examination the tender tube may be felt; tenderness can be produced by moving the cervix. A positive cervical or urethral smear is pathognomonic.

Acute pancreatitis may be either the mild edematous type or the fulminating hemorrhagic type. The pain can be diffuse or it may be located in the back; in the latter case it is usually relieved by sitting up or lying prone. Shock is present early and the pain is extreme. A high blood amylase test corroborates the diagnosis.

Treatment Modern advances in chemotherapy have somewhat altered the treatment of acute appendicitis. Regardless of this fact, however, two schools of thought still exist. One group is of the opinion that acute appendicitis is a surgical condition whenever and wherever seen; the other group advocates conservative therapy in the so-called late or neglected case of acute appendicitis. A practical middle of the road type of therapy can be applied which incorporates some of the tenets of both groups. It is always preferable to remove the leaking focus from the peritoneal cavity; however, there are times and situations when this cannot be accomplished.

A neglected so-called "3 or 4 day appendix" may be associated with a diffuse peritonitis or an early well defined appendical mass. In these two instances the mortality can be lowered if conservative therapy is instituted. Formerly, conservative therapy meant the Ochsner-Sherron regimen namely, Fowler's position, little or nothing by mouth, heat or cold to the right lower quadrant and sedation. Today, however, chemotherapy plays a major role; most cases receive penicillin for its effect upon the streptococci and staphylococci, and streptomycin which affects the gram negative rods. The sulfonamides, sureomycin and chloromycetin also have their advocates. Fowler's position has been discontinued in many clinics; I prefer to let the patient lie in any position in which he is most comfortable. The use of heat or cold over the right lower quadrant is purely a personal problem; either may be used since they act as counterirritants which relieve pain, rather than having a direct bearing upon the appendical pathology per se. In the presence of gastric or small bowel distention gastric siphonage or intestinal intubation is indicated. Protein, carbohydrates, electrolyte, water and vitamin balance must be maintained. Plasma and blood are indicated at times. Sedation is necessary, however, full doses of morphine may mask the picture, hence, I prefer sedatives of a milder nature.

Under such a regimen the neglected case of acute appendicitis will do one of three things: (1) it will get better, (2) it will get worse, and (3) it will form an abscess. There are many ways of determining whether a patient is getting better or worse, since changes in pain, distention, temperature, vomiting and abdominal sounds are all of diagnostic value. However, the one outstanding prognosticator is the pulse. A rule that I have followed and one which has served us well is the following: if the pulse increases twenty beats within an hour and continues to rise, surgical intervention is indicated. This should not be confused with a rapid pulse, in which case conservative therapy is still continued. The pulse is a more sensitive and more accurate indicator than all of the other signs.

If the condition should subside and the patient's condition improve, surgical in-

tervention is delayed for 6 to 8 weeks. To attempt to do an appendectomy 8 to 10 days following a fulminating inflammatory process is to encourage wound infection, herniation, adhesions, fecal fistulae and intestinal obstruction. On the other hand, I feel that it takes approximately 6 weeks for the average inflammatory edema to disappear. If one waits during this interval and then has the patient return for an interval appendectomy the surgery is simple technically, and the postoperative course is usually uneventful. That the patient might have another attack within this waiting interval is possible but most improbable.

If, under conservative treatment, the patient gets worse, the surgeon is forced to operate; these are the cases which are associated with a high mortality. Surgical intervention is considered in the hope that the leaking appendix might be removed. However, these late neglected appendices are usually necrotic and ofttimes cannot be removed: if removal is possible it may have to be done by morcellation. The question as to whether drainage is correct or incorrect in such a case is still controversial. I lean toward the school of thought which believes that the peritoneal cavity is only a potential cavity, and therefore cannot be drained. It has been my custom therefore to close these abdomens without drainage.

The third possibility under conservative treatment for the neglected appendicitis is the formation of an appendical abscess. This is suspected when the patients present a spiking type of fever, chills, sweats and a leukocyte count over 20,000. Should such an abscess form it may get better or it may get worse. If resorption takes place and the inflammatory mass diminishes in size the patient's condition will improve and the mass will disappear. Such a patient is permitted to leave the hospital and is advised to return in 6 to 8 weeks for an interval appendectomy. If, however, the mass enlarges and the patient's condition gets worse the abscess is incised and drained. If the appendix is found in the abscess cavity (this is most unusual) it is removed; if it is not found, an interval appendectomy is performed 6 to 8 weeks after drainage of the appendical abscess. Autoappendectomies have been reported, but these two are quite infrequent.

This plan does not apply to children suffering with acute appendicitis, since it has been shown that children do not have the ability to localize acute appendical lesions. Therefore, in children, the rule must be followed that the case is a surgical one regardless of the time element.

Technical Aspects of Appendectomy The choice of the incision, whether a McBurney or a rectus, will be determined by the type of case and the surgeon's preference.

At times it might be difficult to locate the appendix, however, by following two simple maneuvers the vast majority of appendices can be found readily. The cecum is picked up in a moist laparotomy sponge and gently pulled upward toward the anesthetist. The terminal ileal fat pad (a neglected bit of anatomy which is an excellent surgical guide) is grasped with a Babcock forceps and handed to the assistant at the opposite side of the table. These two simple maneuvers will result in bringing the appendix immediately into view in 85 to 90 percent of cases. Since over 70 per cent of appendices normally lie retrocecally and since the terminal ileum and its fat pad run parellel with the cecum the rationale of these two maneuvers is apparent.

The anatomy of the appendical artery should be emphasized if the serious complication of intra-operative hemorrhage is to be avoided. The appendical artery arises from the posterior cecal branch of the ileocolic artery. The artery to the appendix does not pass retrocecally, but takes a retro-ileal course. If, therefore, hemorrhage from an appendical ar-

tery should take place during the course of an appendectomy the ileal fat pad should be raised and the bleeding point searched for behind the terminal ileum. Retrocecal search for such a bleeding vessel will fail to reveal the source of hemorrhage.

Many methods of management of the appendical stump have been described; these too must remain a personal problem until definite evidence can be produced to substantiate the claim that one method is definitely superior to all the others.

Summary

1. The Two Question Test has been useful in correctly diagnosing most cases of acute appendicitis.

2. The mortality of acute appendicitis still remains high.

3. The fallacy of right rectus rigidity as a diagnostic sign is discussed. The iliopsoas and obturator signs are stressed as signs which locate rather than diagnose an acute appendicitis.

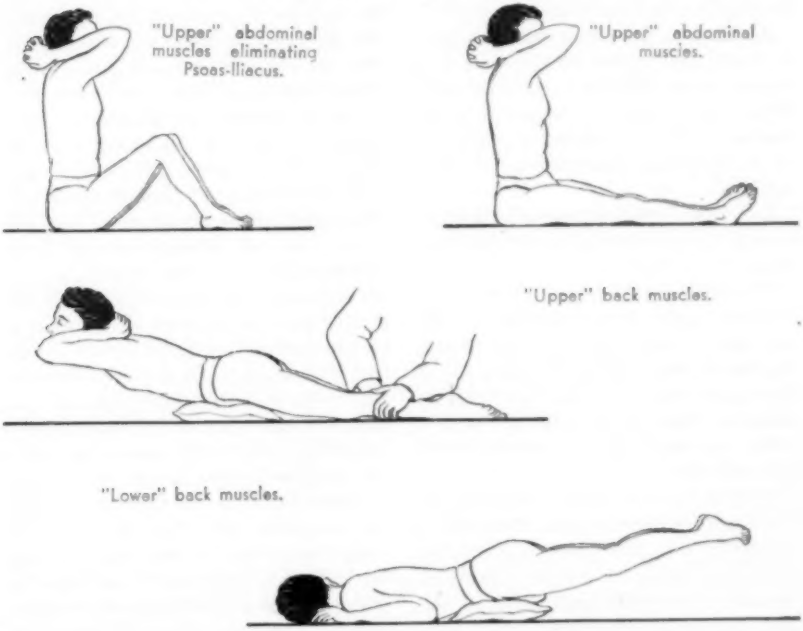
4. A simple method of locating the appendix is presented.

5. A plan of treatment is presented which includes the management of both the early and the neglected case.

25 E. Washington Street

Clini-Clipping

Diagrams showing tests for evaluating the strength of the antigravity trunk musculature.



Nasal Bleeding

MURDOCK EQUEN, M.D.
FRANK BUCKNER, M.D.
GEORGE ROACH, M.D.
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Epistaxis is encountered by the general practitioner in all age groups. It may become a difficult problem and even assume alarming proportions.

Bleeding, from whatever source, must be controlled, its cause instituted, and specific therapy instituted. We will confine our discussion to the immediate problem of controlling hemorrhage.

A. Venous Bleeding The vast majority of epistaxes (about 90%) result from rupture of the delicate, superficial veins which form a plexus in the mucosa of the anterior septum. The control of such bleeding is usually relatively easily achieved by pressure.

1. Pressure applied by thumb and finger for four to six minutes often will suffice.

2. Pack: Pressure may be maintained by inserting moist cotton pladgets snugly into either nostril. Again, added manual pressure hastens clotting. The pack should be removed first from the side that did not bleed. After a short interval, the pack should cautiously be removed from the side that bled.

3. Bleeding may arise deeper in the nasal cavity, where exposure is difficult or impossible. In such cases, an intransal pack is indicated. Such a pack should be carefully introduced, using bayonette forceps, a nasal speculum and a good light. Continuous vaseline gauze strip is the material of choice. Packing both sides of the nose enhances clotting by increasing pressure.

4. In obstinate bleeding arising in the nasopharynx or posterior nares, postnasal pack sometimes combined with intranasal pack is most effective. A small, soft rubber catheter is moistened and introduced into the nose and passed into the pharynx. With the aid of a tongue depressor, Kelly clamp and good light, the catheter is drawn up through the mouth. A roll of gauze, 2x2 or 4x4, depending upon the anatomy of the nasopharynx, is tied with a doubled length of braided black silk. The gauze is moistened and cautiously drawn into the nasopharynx by gently withdrawing the rubber catheter through the nose and guiding the pack with the Kelly clamp. A snug intranasal pack of vaseline strip is then inserted and a second roll of gauze, 4x4, is tied between the two black silk threads. This should be tied with a moderate amount of pressure. One important point, that is often neglected, is the attachment of a second short length of braided silk to the loop which binds the postnasal pack. This strand of silk should extend two or three cm. below the soft palate and be plainly visible when the tongue is depressed. This thread is innocuous and affords a quick and easy means

of removing the postnasal pack, which, of course, is often high in the nasopharynx and may be quite inaccessible.

5. Posture: Inclining the head forward, backward or to the side tends to inhibit venous return, thus increasing venous pressure and prolonging bleeding. The patient should stand or sit erect, allowing the blood to drip from the tip of the nose. Should he become faint or if he is bedridden he should recline with the head elevated, if possible.

6. Apprehension: This often becomes a troublesome component. Blood pressure and pulse rise and bleeding are aggravated. In such cases sedation is very helpful.

7. Chemotherapy such as calcium, vitamin K, etc., aids greatly in many cases where there is deficiency of these elements.

8. Coagulation: After identifying the bleeding point, the following routine usually suffices:

A. Use a small metal suction tip. This may be applied directly to the bleeding point permitting a dry field momentarily. The cautery tip is then placed on the suction tip, thus cauterizing the immediate offending area.

B. Inject a small bleb of Novocain under the mucosa. This is best done by using a long, number 28 needle. Avoid piercing the septal cartilage, which blocks the lumen of the needle.

C. Cauterize in a circle about 1 cm. in diameter about the bleeding point, thus sclerosing all veins supplying the area. It is rarely necessary to cauterize the entire tissue for 2 cm.

D. Instruct patient to anoint the cauterized area three times a day with bland ointment — Bacitracin Ophthalmic Ointment is excellent and convenient. This promotes healing but most important, it prevents crusting. Dried crusts and clots retract and irritate the surrounding tissue. The patient will inevitably attempt to remove theses crusts and in so doing, tear the underlying tissue, thus exciting more bleeding, larger crusts, etc.

B. Arterial Bleeding Arterial bleeding deep in the nasal cavities may result from incomplete cutting of the artery. The elastic fibers retract and hold the defect agape. Should the artery be completely severed, the elastic fibers retract and reduce the lumen to an appreciable degree; complete occlusion by clot is the rule in these cases. This often presents an emergency which defies all of the commonly accepted methods of controlling hemorrhage. In such cases, ligation of the external carotid artery may well prove to be a life-saving measure. It is achieved with relative ease, involves very little hazard and the result is most gratifying.

The following three case reports illustrate the effectiveness of this procedure:

Case 1. Mr. E. H., a vigorous male, aged 40, underwent a submucous resection on February 21, 1951. History and physical examination were irrelevant. Blood pressure 122/84, coagulation time, blood picture and urinalysis showed nothing abnormal.

On the seventh postoperative night he was awakened by nasal bleeding. His nose was packed and he was given supportive treatment. Packing was removed on the third day of his re-admission and he was discharged on the fifth day. He was readmitted six days later, having bled intermittently for three days in spite of packing and general supportive treatment administered by his local physician. Upon his third admission, he was taken to the operating room and all of the packing removed. Rather brisk bleeding was encountered in the left posterior nasal cavity. A snug postnasal pack was introduced bilaterally. Both nasal cavities were packed firmly and postnasal packing was secured to a gauze roll at the anterior nares. He was transfused with whole blood, 500 cc. He continued to bleed through this pack and went into shock. His blood pressure could not be obtained and his veins collapsed. He was taken to

the operating room, in bed, where he remained while the external carotid artery on the left side was ligated, whereupon bleeding was immediately controlled. Packing was removed the following morning and he has not bled to date.

Case 2. Mr. J. E., aged 32, was sent in by his family doctor on March 21, 1951, after having bled at frequent intervals for three days despite packing and usual supportive treatment. On arrival he was quite pale, weak and frightened. His history was significant in that he had been partaking of considerable alcoholic beverages for the past five years and had been on an inadequate diet during this time. The laboratory findings were negative except for the expected low hemoglobin and red count. This patient was also repacked carefully and given supportive treatment mentioned above. He, too, continued to bleed through the pack. Ligation of the external carotid artery was elected in his case before profound shock set in. Pack was removed the following day and when last seen, ten days after the operation, he had had no recurrence of the bleeding.

Case 3. Mr. G. C., age 67, admitted April 22, 1952 in mild degree of shock. There was a pack in his right nostril. He was not bleeding on arrival and had received 500 cc. of whole blood prior to admission. His red blood count was 2,400,000, hemoglobin 6 gms. He received 500 cc. of blood April 23, and shortly a massive nasal hemorrhage ensued. He was repacked and given an additional 500 cc. of blood. He bled again through the pack. His hemoglobin was 7 gms. when bleeding was controlled. He had vitamin K, sedation and all the usual hemostatic aids. On April 24, he began to bleed and became quite apprehensive. He was taken to the operating room where the right external carotid was ligated under local anesthesia. Bleeding stopped when the vessel was tied and has not recurred to date. The nasal pack and accumulated clot and mucus were removed an hour after ligation and he was very grateful for the comfort of a free air way.

Case 4. On May 8, 1952 Mr. M. A., age 69, was admitted after having been treated elsewhere for recurrent, right-sided epistaxis for two days. He was given sedation, intranasal pack and anticoagulants, etc. His hemoglobin on admission was 12.5 grams and his blood pressure was 140/90.

He continued to bleed periodically through this pack and that night a postnasal pack, intranasal pack and anterior pack were applied. He continued to bleed through these packs despite sedation, elevation of the head, etc. He was transfused with 500 cc. of whole blood the morning of May 10, but he continued to bleed. His hemoglobin dropped to 6.5 grams by 10:45 p.m. of May 10, and he was obviously quite weak and feeding became a problem. He was taken to the operating room where the right external carotid artery was ligated under local anesthesia. All packing was removed following this procedure to be sure that the bleeding had been entirely controlled. He was returned to his room where he slept quietly for the first time throughout the night. There has been no recurrent bleeding to date.

Discussion

Indication: Ligation of the external carotid artery is indicated:

1. In nasal bleeding when conservative methods have failed to control hemorrhage;

2. As a prophylactic measure when radical surgery or irradiation is anticipated.

Technique: Under either local or general anesthesia, as indicated, the incision is made along the anterior belly of the sternocleidomastoid muscle at the level of the superior aspect of the thyroid cartilage. This relationship should be established before the head is deflected to the side. Otherwise, the tendency is to make the incision too low in the neck. The muscle is retracted with loupe retractors and the

carotid sheath exposed by blunt dissection. Palpation of the pulsating carotid artery easily identifies it through its sheath; the sheath is entered with caution, the jugular vein is carefully isolated and retracted, thus exposing the carotid. After exposing the bifurcation of the common carotid, the external carotid is easily distinguished by the superior thyroid artery, which is its first branch in the neck. The internal carotid does not give off any branches in the neck. An added precaution is the infiltration of the carotid sheath and bulb with Novocain. This blocks the impulses which arise from stimulation of the carotid body. Circulatory collapse may result from carotid body stimulus in a few cases, especially those who have suffered considerable blood loss. The external carotid is ligated with silver wire when permanent ligation is desired. To control bleeding for a shorter time, it may be ligated with braid silk or even heavy chromic gut. It will eventually recanalize when the silk breaks down.

Hazards: 1. Venous bleeding must be kept in mind. Cutting or tearing of the large, delicate veins may result in air emboli due to the sucking action of the respiratory movements.

2. The vagus nerve must be handled with caution.

3. The hypoglossal nerve often sweeps down into the field and must be kept in mind.

4. Sharp dissection is to be avoided after the skin incision is made. Tissues should be separated with the fingers, the knife handle, or by the spreading action of dissection scissors or Kelly clamp.

Conclusion

Nasal bleeding is a common complaint often demanding immediate attention. The vast majority of cases are of venous origin. Methods that facilitate control of venous bleeding have been listed.

Ligation of one or both external carotid arteries may be resorted to in extreme cases either to combat shock from trauma or operation or as a prophylactic measure to avoid anticipated bleeding in radical surgery or irradiation. The procedure is relatively easy and safe; the result is assured.

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Live Parasitic Worm Found in Eye of Man

The first case of a living parasitic worm beneath the retina of the eye was reported by Dr. Hugh E. Parsons, Tampa, Fla.

Writing in the *Archives of Ophthalmology*, published by the A.M.A., Dr. Parsons stated the worm was found in the right eye of a 25-year-old man, causing a partial loss of vision.

The worm has been seen in many areas of the eye during the three years it has been under observation, Dr. Parsons said. On occasion it has become lost, and frequently several weeks passed before it again became visible.

Various forms of medications and diathermy have been employed in an effort to destroy the worm, but none has proved successful. However, Dr. Parsons expressed the hope that it could be reached safely and destroyed by diathermy needles in the future.

The worm was described as small, white and thread-like; it is non-segmented and tapered at each end. On occasion it is extremely active, with the two ends apparently equally active. Dr. Parsons classified the worm as an immature Ascaris, a type of parasite.

Breech Presentation –Management*

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It has been stated that the management of the breech is one of the best tests of a doctor's obstetrical ability. A reported fetal mortality of 3 to 20 per cent and a general higher incidence of injuries to the maternal soft parts and postpartum hemorrhage seem to support this assumption.

Although the cause of breech presentation is not definitely known, the textbooks for years have listed such reasons as prematurity, placenta praevia, hydrocephalus, multiparity, multiple pregnancy, contracted pelvis, pelvic tumors, etc. as etiological agents. Stevenson[1] points out that these are "disconnected reasons given without regard for underlying functional principles which might exert a standard influence under all circumstances." Some authors group the etiologic factors under two basic "Theories." The first is the so-called "Gravity Theory" and the second, the "Accommodation Theory." Years ago Veit[2], Duncan[3], Schatz[4], and Seitz[5] conducted some classical experiments concerning the effect of gravity upon fetal presentation. Schatz suspended the fetus in liquor amnii and found that the breech always sinks. One would conclude from this that if gravity is the only factor concerned, breech presentation would be most common. The consensus of opinion at the present time seems to discount the gravity theory although it may be a factor particularly in the early months. The accommodation theorists contend that the fetus adapts itself to the inside of the uterus and the various factors in and out of the uterus may influence the fetal position.

Two papers by Vartan[6] which have since been widely quoted and discussed appeared in the English literature in 1940 and 1945. This author contended that the breech presentation was not only common in early pregnancy but normal and that as pregnancy advances, for some unknown reason the fetus will undergo spontaneous cephalic version by about the 32nd week unless something prevents it. He contended that the extended attitude (frank breech) of the legs is a major factor in preventing spontaneous cephalic version. Although Vartan does not seem to think so, it would appear that his theory is of the accommodation variety. Stevenson[1] in his recent article points out that the cornuo-fundal implantation of the placenta can be casually operative in the persistence of breech presentation of the human fetus at or near term in single term pregnancies. His studies of soft tissue x-rays of the placenta with many of the placental sites verified by uterine exploration led him to the conclusion that "cornual implantation of the placenta causes the fundal pole of the amniotic sac

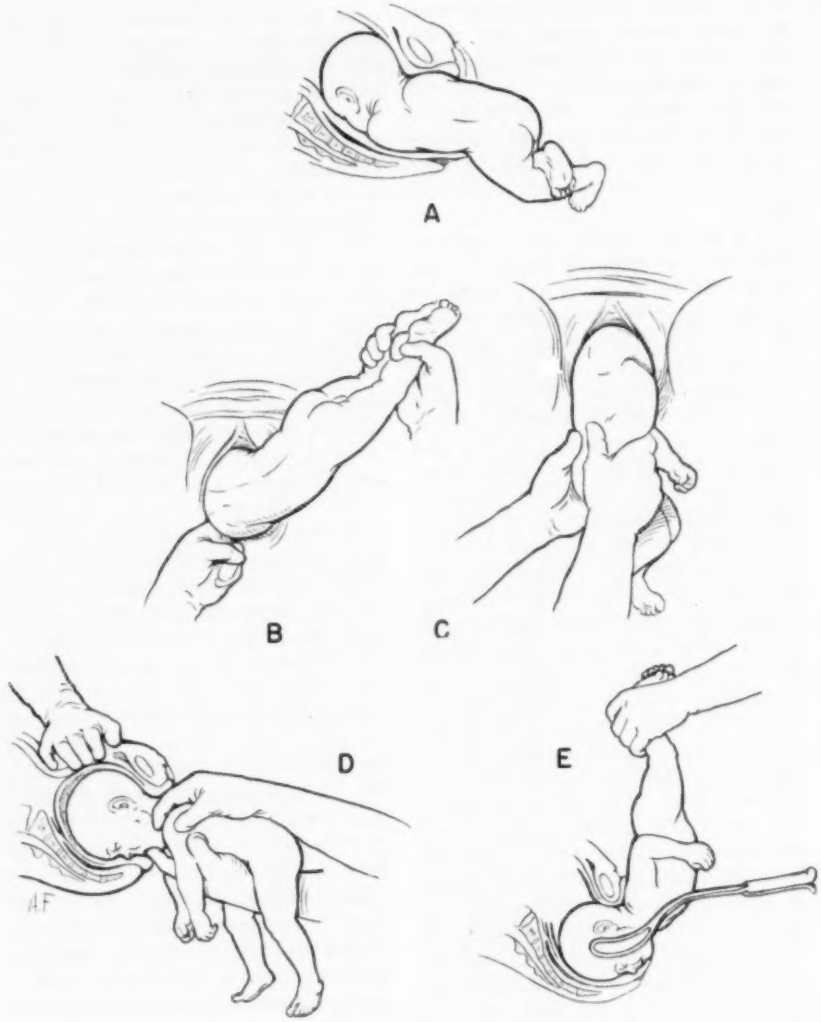
* Some of the material in this article and the illustration appeared in the June, 1951 issue of the West Virginia Medical Journal. Its use in this paper has been sanctioned by that publication.

to have relatively the same size or capacity as, or even a smaller capacity than, the lower uterine segment pole of the sac. Since the fetal head is smaller than its breech and legs, the head will tend to accommodate itself to the smaller pole of the amniotic sac ovoid while the breech will tend to accommodate itself to the larger lower uterine segment of the sac."

In a previous article[7] it was suggested that perhaps in the early months of pregnancy because of the greater weight of the buttock (Schatz), the fetus presents by the breech. As pregnancy advances, we know that for some reason the breech presentation decreases. Weisman[10] made x-ray studies from the twentieth week of pregnancy until term and showed that from the 18th to the 22nd week, 24 per cent of the fetuses present by the breech. This incidence decreases to 8 per cent by the 28th to 30th week and to 7 per cent by the 34th week. At term we know that the incidence is about 3 per cent. Possibly the weight of the head increases and tends to favor spontaneous cephalic version. Suppose that this process of spontaneous cephalic version continues and by the 32nd week all of the fetuses have undergone spontaneous cephalic version unless something has prevented this process. Some of the interfering factors may be: 1. The extended attitude where the legs of the frank breech splint the body and prevent version. 2. Small amount of amniotic fluid (this condition may be a factor in causing the frank breech). 3. Cornuo-fundal implantation of the placenta (Stevenson) making the fundus the smaller pole, thus the head which is smaller than the breech and legs is maneuvered into the fundus, and 4. Bicornate uterus, tumors, multiple pregnancy, etc. The accommodation factors, of course, do not exert as much influence in the multiparous patient as in the primiparous. This may account for the decreased incidence of breech presentation in the multiparous.

As a corrective measure for this undesirable situation, external cephalic version has been suggested. Ryder[8] wrote an excellent article on the subject. In reviewing this and other material, it is interesting to note that even after numerous versions, the incidence of breech delivery at term is still in the neighborhood of 3 per cent. Previously[7] the writer reported a personal experience with external cephalic version in 100 consecutive breech presentations. Even after accomplishing sixty (60%) successful external cephalic versions with sixteen (16%) spontaneous reversions, the over-all incidence of breech presentation at term was still 4.8 per cent. This figure, which is somewhat higher than the general reported incidence of about 3 per cent, was accounted for by the fact that most of these 100 cases of breech presentation were seen in two clinics which received a large number of breech referrals. Recently[9], we have been doing routine x-rays on consecutive obstetrical patients at 24, 28, 32, and 36 weeks of pregnancy. No attempt to do any external cephalic versions has been made. In reviewing the films on some eighty patients completed to the time of this writing, a high early 20 per cent incidence of breech presentations was found, which progressively decreased by spontaneous version to about 3 per cent at term. These figures closely parallel those of Weisman.[10]

These findings suggest, as Vartan[6] and others have pointed out, that spontaneous versions will take place unless something prevents it, and in those series where a large number of external cephalic versions have been done, spontaneous versions would have taken place in most cases if the patients were let alone. With this thought in mind, it seems that even though the technic of external version should be mastered and practiced in selected cases and, of course, in transverse positions at or near term, the maneuver cannot be



(A) Delivery allowed to proceed spontaneously until at least umbilicus is born. Favor downward traction until at least lower half of the scapulae are outside of the vulva.

(B) Some free posterior shoulder first because of greater space in the posterior and lateral segments of the pelvis. It is better to free the shoulder which has a tendency to be born spontaneously.

(C) Anterior shoulder delivered by downward traction. Suprapubic pressure maintained by assistant to prevent extension of head.

(D) Infant's body rotated to bring sagittal suture in the A. P. position. Head delivered by Mauriceau maneuver combined with suprapubic pressure.

(E) If delivery is not accomplished easily Piper forceps applied.

relied upon to eliminate the breech at term. Therefore, it appears that in order to reduce the infant and maternal mortality and morbidity, we must examine and improve our method of conducting the breech delivery.

There are some who advocate and practice extraction as soon as the buttock is visible at the vulva. Others do not wait this long but perform this operation as soon as the cervix is dilated. Potter[11] for many years did hundreds of versions and extractions on women with perfectly normal cephalic presentations. His primary indication was to eliminate the "pains and agonies of the second stage of labor." It is hard to believe that operative deliveries of this type do not damage the infant despite claims to the contrary.

A strictly conservative attitude in handling these cases would be, of course, complete noninterference allowing the patient to deliver entirely spontaneously without any traction being employed and without any manipulation other than support of the infant. If the physician is patient, this procedure can be followed in a surprising number of multiparas, but in general the partial breech extraction is advisable in most primiparae and in those multiparae where some delay is encountered. Partial extraction consists of expulsion of the infant as far as the umbilicus by natural forces with the remainder of the body then extracted by the attendant.

Because a breech labor usually is longer than that in cephalic presentation, it is important to make the patient as comfortable as possible. In attaining this end, gaining and holding the confidence of the patient and family are probably more important than the administration of drugs. Read's[12] successful practice of natural childbirth is built almost entirely on this principle. Many times a screaming patient and an edgy family pressure the physician to interfere and endanger mother and child.

On admission of the patient in labor the writer usually administers Seconal, gr. 3 and Demerol, 100 mg. After the patient has been prepared and an enema given, the examination is conducted. If everything is satisfactory, the patient is assured and such statements as the baby is upside down and others of like nature are avoided. She is told approximately when the baby will be born and assured that as her contractions become stronger, sufficient medication will be administered to keep her comfortable. At necessary intervals Demerol in 100 mg. doses is administered. As much as 400 or 500 mg. are administered during a long labor. Additional Seconal usually is avoided because from clinical observation this seems to depress the infant more than the repeated doses of Demerol. The patient is encouraged to sleep and the family to stay in the waiting room. When delivery is imminent, the patient is transferred to the delivery room. She is further encouraged and told to bear down with her contractions. If an episiotomy is deemed necessary, as soon as the buttock "crowns" the perineum is injected with 1% Novocain. This operation is usually advisable in the primipara because it not only protects the mother from extensive tears, but facilitates delivery, especially of the aftercoming head. In many multiparae the episiotomy can be omitted provided the buttock is allowed to distend the perineum completely. Delivery is permitted to proceed spontaneously until the umbilicus has been born. It has frequently been stated that not more than eight minutes should elapse after this stage for completion of delivery if a live baby is to be expected. This is not quite true. Furthermore, eight minutes is quite a long time and frequently the shoulders can be delivered spontaneously and the head leisurely extracted in less than five minutes. The arms are normally crossed over the chest. If traction is started too soon, the arms go up around the head and interfere with easy delivery.

Also, the flexed head aids materially in delivery. This is disturbed by premature traction. Flexion can be maintained by having the nurse maintain downward pressure on the fundus as soon as the breech begins to emerge from the vulva. It is important to favor downward traction until at least the lower halves of the scapulae are outside of the vulva and not to worry about delivery of the shoulders until one of the axillae becomes visable. Although there is more space in the posterior and lateral segments of the pelvis than in the anterior and some men always attempt to free the posterior arm first, as long as the arms maintain their normal flexed attitude over the chest, it is better to free the shoulder which has a tendency to be born spontaneously. After delivering the shoulders, the body is then rotated so that the sagittal suture is in the anterior-posterior, preferably with the face down. If the head cannot be delivered by a very gentle Mauriceau maneuver combined with suprapubic pressure, the Piper forceps should be applied to the aftercoming head. In spite of the fact that the Mauriceau maneuver has been termed by some as obsolete and the cause of fracture of the clavicle, hematoma of the sternocleidomastoid and Erb's paralysis, it is important that one be familiar and experienced with the maneuver. Gently performed, it is as safe and many times more safe than forceps. Then too, satisfactory instruments may not always be available.

Nothing has been said about auscultation of the fetal heart tones. This, of course, should be done after every pain before the breech is expelled from the vulva since this is the best way of detecting fetal distress which may necessitate extraction. However, one should become experienced in listening for the heart tones because they are at times difficult to hear on account of rotation of the baby's body, thick abdomen, etc. Nothing has been said about the special maneuvers used in delivering the breech. In practice these are needed only occasionally and are described in detail in the textbooks.

In conclusion, conservatism in conducting these cases should be emphasized. We should constantly keep in mind that childbirth is a normal function and, as such, nature has made provisions for the fulfillment of this function, regardless of the presentation. Obstetrical deliveries cannot be scheduled like elective surgery or arranged so that they will not interfere with our social activities. Honest, interested experience in obstetrics soon teaches one that the less we interfere with these patients, the better our results.

Summary

1. In breech presentation a higher fetal and maternal mortality and morbidity rate is encountered than is the case in cephalic presentation.

2. Although definitely of value, external cephalic version cannot be relied upon to eliminate the breech at term.

3. In delivering these cases conservatism is recommended. Complete extraction should not be a routine procedure. A "relaxed" partial extraction is much safer for mother and infant.

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Atherosclerosis
Thesis and Hypothesis

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From the standpoint of morbidity and mortality, arteriosclerosis is probably the most important disease problem in this country today.[1] The research and reports in the literature concerning this disease and its pathogenesis are myriad. Most of the recent reports are concerned chiefly with atherosclerosis or atheromatosis which appears to be the most important type of arteriosclerosis in so far as morbidity and mortality are concerned.

Atheromatosis is a disease of the intima most often seen in the aorta, but frequently found in the cerebral, coronary and renal arteries. The characteristic lesion is a sub-intimal collection of lipid-laden foam cells.[1] Deposits of lipids, the formation of fibrous plaques and atheromas and the deposition of calcium in the aorta and its branches are the dominant changes of atherosclerosis. Initial growth manifestations of this disorder are fatty streaks, or small nodules in the root, arch, and posterior wall of the aorta, especially about the ostia of the intercostal arteries and other branches. Growths of fibrous tissue in these fatty deposits form larger discrete and confluent lesions. These lesions which may enlarge by the accumulation of more foam cells, may become necrotic and ulcerate through the overying intima and may slowly regress, the foam cells being replaced by varying amounts of connective tissue. Later with necrosis, the centers soften and become masses of soft lipid material and tissue debris, the atheromas. When the lining edge of the atheroma breaks, the lesion becomes an atheromatous ulcer.[2] Injury of the endothelium favors thrombosis.

Complete descriptions of the gross and microscopic findings in the aorta and arterial tissues have been published by Marchand, Duff, Leary, Aschoff, and Frey.[3, 8, 12] Microscopic examination of early fatty streaks discloses swelling and increase of the intima metachromatic ground substance in which fine droplets of sudanophile-lipid material are scattered; subjacent elastic lamellae also may be mantled with minute droplets of lipid. Intracellular accumulations are found in lipid-filled globular macrophages (foam cells) and in spindle-shaped or stellate mesenchymal cells in the intima. The latter are best seen in sections paralled to the intimal surface.

As the lesions advance, fibrous proliferation becomes more prominent in their superficial layers while there is a concentration of lipid-filled foam cells in their deeper parts. The fibrous cap thus formed over the main lipid accumulation exhibits excess quantities of metachromatic ground substance, varying degrees of hyalinization and sometimes fibrinoid necrosis.[3]

The lesions seem to vary somewhat depending upon the age of the artery and the rapidity with which the lesion develops. Leary points out that in the young human being progressive fibrosis is the usual picture with narrowing of the coro-

nary lumen.[4] Lipoid cells filled with cholesterol esters are deposited in the intima beneath the endothelium, but are replaced by young fibrous tissue before any considerable accumulation of these cells can occur. The deposit of lipoid cells is progressive or cyclic and a growth of young connective tissue replaces them, pari passu, until the lumen is markedly narrowed. Russell L. Holman agrees that from his studies thus far made it would appear that in all forms of arterial lesions, both human and experimental, there is good evidence of their development by episodic stages, and the tempo of the episodes is more in keeping with days than it is with decades.[5]

Leary further shows that, in the aged, large collections of lipoid cells arise with a minimum amount of fibrous tissue support. The delicate fibrous tissue partition between these cells is dependent upon lymph, or plasma diffusion by imbibition through the endothelial layer from the blood in the arterial lumen. As the cells accumulate, the nutrition of the cells tends to suffer and massive necrosis occurs, followed by liquefaction producing so-called atheromatous abscesses.

There are other differences in the lesions, depending on whether they develop spontaneously or are brought about by artificial means, such as prolonged cholesterol feeding, thyroidectomy, thiouracil, pancreatectomy, etc. The development of the lesions is more rapid in individuals with certain other disease states such as hypothyroidism, the nephroses, diabetes mellitus, and familial hyperlipemia and hypercholesterolemia that are characterized by a high cholesterol level of the blood plasma. The development of the lesions is deterred by many things such as thyroid extract, heparin, certain detergents, notably Tween 80 and Triton A-20, as well as alloxan diabetes in the rabbit.[6]

The many facts which are known about atherosclerosis have been subject to the most varied interpretations. This has resulted in many widely divergent concepts of pathogenesis. The first concept long held was that atherosclerosis was a progressive and irreversible affection of the arteries, associated with the normal aging process.[7] More recent evidence tends to show that atherosclerosis is a reversible process and not necessarily associated with aging.[8, 9, 10, 11, 12] "The lipoid infiltration of the arterial intima and sub-intima, which constitutes the basic pathologic lesion of atherosclerosis, is variously regarded as due to imbibition from the blood stream; as the result of invasion of the sub-endothelial layer of the artery from the blood stream by foam cells, lipoid-laden macrophages wandering from the liver,[13] as a consequence of extravasation of serum and of hemorrhage from the arterial vasa vasorum;[14,15] as a necrotic-debris of degenerated subintimal tissue[16] and as due to local production of lipid consequent upon disorganization of the intima resulting from mechanical strain of the arterial wall.[17, 18]

Cholesterol Interest in the relationship of cholesterol to the development of atheromatosis dates from the demonstration by Aschoff more than forty years ago that large amounts of cholesterol and other lipids are present in the atheromatous lesions of the aorta and its large branches. This interest was greatly intensified by Anitschkows' report in 1911 of experimental production of atheromatous lesions in rabbits by feeding cholesterol for long periods. Anitschkows' observations have been abundantly confirmed and a voluminous literature has accumulated on this subject.[19–51]

The fundamental role of serum lipids is emphasized by the experimental production of atherosclerosis in the rabbit, guinea pig, chicken and dog by sustained elevation of blood cholesterol. In the dog, it has been found necessary to combine thiouracil administration with the cholesterol feeding to produce atheromata. The lesions thus produced resemble human

atherosclerosis in distribution and character.[52, 53]

The significance of the role of hypercholesterolemia in the development of atherosclerosis is the subject of much debate. Peters and Van Slyke feel that no general disturbance of lipid metabolism has been demonstrated in patients with atherosclerosis.[54] Numerous investigations have failed to demonstrate that hypercholesterolemia is essential to the development of human atherosclerosis. "Indeed, in the vast majority of cases with or without clinically demonstrable atherosclerosis, the blood cholesterol is normal."[55] Lande and Sperry compared the total lipid content of the aorta at autopsy with serum cholesterol of patients who had died suddenly, in most instances with trauma. No relationship was established.[56]

On the other hand, according to Ancel Keys, significant inferences can be made from indirect evidence, if we admit that there is an important relationship between atherosclerosis and the concentration of chloresterol in the serum. There is overwhelming evidence for such a relationship:

(1) On the average, whenever the serum cholesterol tends to be high, as in diabetes, nephrosis, hypothyroidism, and idiopathic hypercholesterolemia, there is a tendency toward early and severe atherosclerosis.

(2) Persons with definite evidence for disease of the coronary arteries tend to have elevated serum cholesterol values, especially when they are compared with properly matched "normals." Good confirmation can be obtained from recent raw data.

(3) There is at least some parallelism between the age trend of cholesterol concentration in the serum and the age trend in atherosclerosis development.

(4) In animal experiments there is a close parallelism between the serum cholesterol level and the development of experimental "atherosclerosis."[57] In a recent study employing the Schoenheimer-Sperry method of blood cholesterol determination, which is more accurate than older methods, Morrison, et al., reported that sixty eight percent of seventy five patients under sixty years of age with coronary occlusion exhibited hypercholesterolemia, with levels of blood cholesterol exceeding 260 mgms. per cent.[58] Particularly significant is the demonstration of hypercholesterolemia in young individuals with coronary artery disease, subjects in whom other factors contributing to the development of arteriosclerosis are lacking.[59, 60]

It has been observed that not only are the levels of cholesterol elevated in subjects with coronary atherosclerosis, but the serum cholesterol also fluctuates widely, contrasting with the relative stability of the serum cholesterol in normal individuals.[61] Moreton has suggested that the recurrent hypermacro-chylomicronemia observed after fat meals may be responsible for the development of atherosclerosis.[62] This hypothesis would favor the episodic development of the lesion.

There is a considerable amount of clinical and pathologic data that tends to show that obese or overweight individuals are more prone to atherosclerosis and its consequences.[63, 64, 65] Thin undernourished persons tend to have somewhat less atherosclerosis than might be expected.[66, 67] Firstbrook has recently advanced experimental data that appear to show that a lesser degree of atherosclerosis develops in undernourished rabbits during a course of cholesterol feeding than in the corresponding well nourished control animals.[68] In view of this confusion it appears obvious that other factors are involved in the development of atherosclerosis and many of them have already received careful study.

Age Brief reference has already been made to the effect that the development of the lesion of athrosclerosis is affected by the age of the artery in which it develops.[69] Despite this effect of age, Leary

concludes that atherosclerosis is a disease and not the inevitable consequence of age and since it occurs in early life and is frequently highly selective in its localization, that the process is metabolic and not inflammatory. There is some evidence to the effect that cholesterol may act as a low grade irritant, resulting in the fibrous tissue development. Wilkinson, *et al.*, calls attention to the fact that all of the experimental methods for producing atheromatosis work as well in the young and middle aged animals as they do in the older animals. They report a case of a girl nine years old with angina pectoris, which presumably was due to advanced atherosclerosis. They conclude that the development is an episodic process and feel that the fact that it occurs more commonly in older than in younger people may be the result of an accumulation of lesions over a period of years rather than being due to a process that is associated with old or middle age.[1]

The concept of cholesterol age is presented by Gertler, Garn and Bland on the basis that a patient with coronary heart disease at 25 has a serum cholesterol similar to a normal male at the age of 45. Since there is a rise in cholesterol with age in both groups and since there is a significant correlation in one, and a possibly significant correlation in the other, "it seems likely that age and cholesterol, are covariant." At every age level between the third and sixth decade, the coronary disease group has markedly higher and more variable serum cholesterol levels than the healthy group.[70]

Gubner and Ungerleider state "the mechanisms for the removal of lipoid from the arterial wall are not adequate to dispose of the lipoids constantly penetrating through the endothelial membrane." Over the span of decades, increasing accumulation of lipoids occurs in regions where the sub-intimal tissue spaces are most abundant, with the development of atherosclerosis in progressively increasing degree with advancing age.[71, 72, 73, 74, 75, 76] Such increases in concentration of lipoids lead to their precipitation for the concentration of cholesterol in the blood stream in man is at a level not far from the point of saturation.[77]

There is a broad basic pattern of changes in the inter-cellular environment common to all aging tissue. Basically, these changes consist of an accumulation and alteration in the colloidal constitutents of the intercellular fluid. The accentuation of such age changes in the artery is to be attributed to the uniqueness of the factors determining its inter-fluid formation and circulation, i.e., the high vascular filtration pressure which greatly increases the filtration of colloids from the blood stream across the endothelial membrane. The cholesterol content of the normal aorta increases with age, the increment being accentuated in individuals with hypertension, i.e., heightened vascular filtration pressure.[78, 79, 80] Hyptension then is sometimes considered as a cause[78] and sometimes a consequence of atherosclerosis.[7, 81, 82]

FACTORS INVOLVED IN THE TRANSPORT OF THE LIPIDS AND OR CHOLESTEROL THROUGH THE ENDOTHELIUM AND THEIR DEPOSITION IN THE INTIMA

(1) There has been much discussion concerning the manner in which the lipids and cholesterol reach the intima and are deposited there. Most authors seem to agree that the cholesterol in large part passes or is brought through the endothelium into the intima from the plasma in the lumen of the vessel. The inner layers of the arterial wall, including most of the media, derive their nourishment from the blood flowing within the lumen of the vessel, for the most part, by direct diffusion across the intact endothelial membrane. The studies of Petroff, Lang, Anitschkow, Iwanov, indicate that normally a constant stream flows through the walls of the large artery in the direction from lumen to ad-

ventitia. Water, salts, dextrose and other blood constitutents enter the sub-intima tissue spaces, in the course of the nutritive process to the vascular wall. The lipoids, too, penetrate the intima and are transported through the media to be removed by the lymphatics of the adventitia. After passing through the endothelium, the blood transudate, i.e., intercellular fluid, penetrates the entire thickness of the arterial wall.[71]

Duff, MacMillan, *et al.*, state that "almost nothing is known of the means by which lipids enter the arterial intima or how they become fixed there." There is a good reason to believe that they infiltrate the intima from the blood plasma, but in what form they enter or by what mechanism they are transferred and how they are accumulated or removed is obscure. The accumulation of lipids in the intima probably is the result of the preponderance of a group of general and local factors favoring the deposit and accumulation of lipids in the intima over another group of factors that favor their mobilization and removal. On the other hand, preponderance of the latter group of factors over the former would account for the diminution of lipid accumulations during periods of retrogression of the lesions. The clear recognition and understanding of all the factors concerned in the etiology and pathogenesis of atherosclerosis must await the future.[83]

Gubner and ungerleider feel that the simplest and most reasonable view is that of direct imbibition of lipids from the plasma together with other plasma constituents through the intima endothelium under the influence of the high filtering arterial pressure. Chemical analysis indicating that atheromas are not constituted of cholesterol alone, but contain the same lipids as are present in plasma, supports this concept.[71, 84, 85]

Heuper suggests that a disturbance in the colloidal stability of the serum lipids may result in deposition of a film of macromolecules on the endothelium, resulting in interference with the oxygenation. Anoxia leads to increased permeability of the endothelial membrane and the deposition of lipids and lipid-laden cells in the intima. In support of this hypothesis Hueper produced lesions resembling experimental cholesterol in human atherosclerosis by the injection of a variety of macro-molecular colloidal carbohydrates, such as polyvinyl alcohol, methyl cellulose, pectin and acacia. Moreton's theory of temporary macrochylomicronemia fellowing the ingestion of fatty meals has been mentioned.

Leary has proposed the theory that the atheromatous process is the result of an invasion of the intima by macrophages from the blood stream across the endothelial membrane. These macrophages bear lipid material and are termed by the author lipophages. He has demonstated all phases of the invasion. The work of Simonton and Gofman seems to indicate that macrophage migration with special reference to Kupffer cells is not a significant sources of the foam cells in rabbit atherosclerotic lesions.[86] Duff has observed that anisotropic lipoid appears extracellularly in the intima before any fat containing cells are to be found.

Gofman and his associates have presented important evidence relating certain serum lipoproteins to the development of atherosclerosis.[87, 88, 89] Further studies now enable them to make quantitative estimation of the relationship of certain aspects of lipid transport via lipoproteins with atherosclerogenesis.[90] They conclude that (1) A variety of serum lipid disturbances experimentally induced in the rabbit, some of which are associated with the development of atherosclerosis, have been analyzed. The Sf 10-30 class of lipoproteins, which develops in the rabbit in certain of these experimental procedures, is highly associated with and universally concurrent with the development of atherosclerosis, independent of the type of metabolic disturbance experimentally induced. The normally occurring

lipoproteins (Sf 10 and less), even when elevated experimentally show no significant positive association with atherosclerosis. Certain other cholesterol-bearing lipoproteins (Sf 100 and higher) are either not associated with atherosclerosis or are inversely associated with atherosclerosis.

(2) In the rabbit, total serum cholesterol levels, considering as a group all of the types of induced lipid metabolic disturbances, are either unrelated to the atherosclerosis, or may be inversely associated with atherosclerosis. Only under the special condition where a major fraction of the cholesterol is in the Sf 10-30 class of lipoproteins does total serum cholesterol correlate well, positively, with atherosclerosis.

(3) An estimate of the quantitative association of the Sf 12-20, Sf 20-35 Sf 35-100 lipoprotein classes and of total serum cholesterol with atherosclerogenesis in the human has been made, studying each on the same serum sample from a given individual. Patients with coronary artery disease have served as a criterion group for the atherosclerotics. Throughout the entire age range evaluated, from 41 to 60 years, the Sf 12-20 lipoprotein levels show at least a twofold and up to a possibly tenfold higher relationship with atherosclerosis than does the total serum cholesterol. The Sf 20-100 lipoproteins (containing the Sf 20-35 class plus the Sf 35-100 class) also show a correspondingly higher relationship with atherosclerosis than does the total serum cholesterol. The Sf 12-20 lipoproteins and the Sf 35-100 lipoproteins are partially intercorrelated; but each shows, in addition, strong independdent associations with athersclerosis. The Sf 20-35 lipoproteins show a lesser association with atherosclerosis than either of the other classes and, further, much of the association that is present depends upon partial correlation of the Sf 20-35 lipoprotein with either Sf 12-20 or Sf 35-100 or with both.

The Sf 12-20 and Sf 35-100 lipoproteins show strong association with atherosclerosis, regardless of age or total serum cholesterol level. Thus, even for individuals with the same total serum cholesterol, be it low, moderate, or high, there is strong ability of the Sf 12-20 and SF 35-100 lipoproteins to segregate atherosclerotics from normals.

Total serum cholesterol shows a much lower ability to segregate atherosclerotics from normals in the 41 to 50 years age group than the Sf 12-20 and Sf 35-100 lipoproteins. In the age group 51 to 60, while the lipoproteins maintain their strong association with atherosclerosis, there is only a borderline ability, if any, of the serum cholesterol to segregate atherosclerotics from normals.

(4) What little association total serum cholesterol does have with atherosclerosis is wholly due to its partial correlation with the Sf 12-20 and Sf 20-100 lipoproteins, which are strongly associated with atherosclerosis. In essence, this means that approximately 10 percent of the serum cholesterol is important for atherosclerosis (namely, the fraction in the Sf 12-20 and Sf 20-100 lipoproteins), while the remaining cholesterol is unassociated with atherosclerosis. As a result of the fact that the vast bulk of the serum cholesterol is in nonatherogenic lipoproteins, the measurement of total serum cholesterol in an over-all way does more to obscure the atherosclerotic potentialities of an individual than to clarfy them.

(5) Even marked hypercholesteremia is not uniformly associated with atherosclerosis. Groups manifesting advanced atherosclerosis (including patients with coronary disease or xanthoma tuberosum) are strikingly segregated from equivalently hypercholesterolemic individuals without manifest atherosclerosis by the Sf 12-20 and Sf 35-100 lipoprotein measurements.

(6) The crude estimate of the factors which segregate atherosclerotics from normals, based upon biserial correlation, indicates that the combined Sf 12-20 and Sf

35-100 lipoproteins account for at least 35 percent of the total etiologic factors. When the impurity of the normal population (i.e., admixture with atherosclerotics), the fallibility of diagnosis in the criterion group wtih coronary disease, the focal factors in atheroma formation, the difference between accumulated atherosclerosis and atherosclerotic activity and the biologic and technical variation of measurement are all taken into consideration, the combined Sf 12-20 and Sf 35-100 lipoproteins will account for at least 75 to 80 per cent of the total variation between atherocleroties and normals, and may very well account for the entire difference.

(7) Follow-up studies have shown that early recurrence of myocardial infarction in patients with coronary disease is positively and highly related to the Sf 12-20 lipoprotein levels. The recurrence rate of myocardial infarction is approximately 20 per cent per year for those patients with Sf 12-20 levels of 100 Mg. per 100 cc., whereas the recurrence rate is approximately 6 per cent for those patients with Sf 12-20 levels of 50 Mg. per 100 cc. It may be that when the combined Sf 12-20 and Sf 35-100 levels are evaluated, the relationship of recurrence with lipoprotein level may become stronger.

(8) The occurrence of myocardial infarction, de novo, in normals is positively related to elevation in Sf 12-20 lipoprotein levels.

(9) The depression of high Sf 12-20 levels by dietary restriction of fat and cholesterol has been shown to decrease significantly the chance of recurrence of myocardial infarction in patients with established coronary artery disease. At this time a significant statement on the point of dietary protection can be made on a follow-up of high level patients with coronary disease (above 80 Mg. per cent of Sf 12-20) only because their recurrence rate has provided significant data in a short period.

(10) The demonstration that the Sf 35-100 lipoproteins, in addition to the Sf 12-20 lipoproteins, are associated with atherosclerosis, is of especial significance with respect to the ingestion of fat. This class of lipoproteins, the Sf 35-100 class, may be raised acutely in a high proportion of humans following ingestion of fat. In patients with a severe degree of the lipid metabolic derangement which leads to "abnormal" lipoprotein patterns, this Sf 35-100 class of molecules is sustained even postabsorptively. It appears, since we have already demonstrated that a dietary lowering of the Sf 12-20 lipoproteins has an ameliorative effect on coronary disease based upon atherosclerosis), that dietary fat restriction is equally important, by way of depressing the Sf 35-100 level, in the effort to control atherosclerosis.

(11) The rating of a patient with respect to atherosclerogenic potentialities is best achieved by a measure of the levels of Sf 12-20 lipoprotein and Sf 35-100 lipoprotein. Of the two measures, the Sf 12-20 level is the more stable, not being acutely influenced by diet. The Sf 35-100 level, even though more variable acutely with diet, is nevertheless highly associated with atherosclerosis and provides valuable additional assessment with regard to atherosclerogenesis. Thus we may regard the SF 12-100 lipoproteins as the "atherosclerogenic band" of the serum lipoproteins. The exact assessment of relative atherogenicity of each subsegment within this region is not now possible, so that for the present, classification is made without weighting within this region.[91]

In a recent study Ahrens and Kunkel[92] called attention to the importance of the phospholipids in the stabilization of serum lipid emulsions. Some sera with high total lipid content may be perfectly clear whereas others, with similar or even lesser lipid content will be quite turbid or milky. The physical difference between the two types lies in the lipid particle size; particles with diameters less than one quarter the wave length of visible light (or 0.1

micron) will not be seen in the visible light range and the containing serum will be clear, whereas larger particles by interrupting light rays give the serum the appearance of turbidity. Analysis of such pairs of sera demonstrated that the important difference lay in the phospholipid: total lipid ratio, for example a serum containing 2.969 mgms. of total lipid of which 1.400 mgms was phospholipid (ratio -0.47) was quite clear in contrast to another, markedly turbid, in which the total lipid content was only 1.128 mgms. and phospholipid 312 mg. (raio -0.28) A clear high lipid serum could be made turbid by destroying the lecithin with lecithinase. It was not possible, in vitro, to increase the clarity of milky serum by increasing its phospholipid content.[93].

The possible relationship of this physical-chemical phenomenon to the pathogenesis of atherosclerosis has been stressed in several recent studies. Kellner, *et al.* found that cholesterol fed rabbits which also received intravenous injections of the surface-active agents Tween 80 or Triton A20, developed a sustained hypercholesterolemia and yet failed to develop as great a degree of atherosclerosis as those animals receiving only cholesterol. Chemical analysis revealed that the former group had a proportional rise of both cholesterol and phospholipid while the latter showed a disproportionate increase of cholesterol.[94]

Recently there has been a revival of interest in the observation of Boyd that phospholipids play a role in the stabilization of the plasma lipid emulsion. Serum cholesterol exists in large molecular colloidal aggregates or miscellae[95, 96, 97, 98, 99] in close association with the serum proteins particularly the globulin fractions. Ludlum, Taft and Nugent believe from their studies of the tiny particles of lipid in the blood that the particles are stabilized by a protein film because the first zone of aggregation of the particles occurred at a pH range of 4.7 to 5.3, approximately the iso-electric points of albumin and globulin, and the droplets coalesced when the acidity was sufficient to precipitate the protein and destroy the film. The membrane about globules of fat in milk, according to Palmer and Weiss, is a mixture of protein and phospholipid. Churning of the milk removes the membrane. The degree of dispersion of the lipid material and the particulate size facilitate or deter this process. Tissue utilization of hydrophylic colloids such as protein and lecithin which hold the hydrophobic cholesterol in colloidal dispersion may lead to precipitation in the arterial wall.[100]

Most atherosclerotics exhibit plasma cholesterol values well within the normal range but show disturbances in cholesterol phospho-lipid ratio. Barr and his associates found that a high percentage of alpha-lipoprotein, such as is found in normal young women, will tend to produce a relatively low cholesterol phospho-lipid ration in the plasma and that the low values of alpha-lipoprotein in atheroma in kindred conditions will tend to increase the ratio.[101] The outstanding fact in their observations is the relative and absolute reduction in alpha-lipoprotein in atherosclerosis and kindred conditions. This is particularly apparent in the hypercholesterolemic states of nephrosis and xanthoma tendinosum in which, in spite of enormous increases in total cholesterol, the concentration of alpha lipoprotein may be much less than in normal individuals. Under such circumstances there is always a relative and absolute increase in the concentration of beta lipoproteins. It is suspected, although as yet not proven, that the Sf 10-20 molecules of Gofman form a part of the beta lipoprotein increment.

In speculating upon possible mechanisms it has occurred to us that presence in higher than normal concentration of beta lipoproteins may in itself be significant in the genesis of atheroma. Furthermore, it might be suspected that all of the group rather than the small fraction of Gofman's Sf 10-20 contributes to a tendency to

instability of lipid emulsions in plasma and tissue fluids. They conclude:

1. Patients who have survived coronary occlusion or present otherwise unequivocal evidence of the complications of atherosclerosis frequently exhibit several abnormalities in the distribution of proteins and lipids in the plasma. These include a tendency to reduction of albumin and alpha lipoprotein and a relative and absolute increase in beta lipoprotein, as well as other components of Cohn's Fractions I and III.

2. These changes may be apparent without hypercholesterolemia or recognizably significant elevation of the cholesterol-phospholipid ratio of the unfractionated plasma. Like normal individuals, patients in the atherosclerotic group exhibit, in the fraction containing alpha lipoproteins, cholesterol-phospholipid ratios which average around 0.50 and in the fraction containing beta lipoproteins ratios which range about 1.40.

3. Similar changes in protein and cholesterol distribution are apparent in conditions which are known to predispose to early and extensive atherosclerosis. In many diabetics they are apparent before any vascular complications of the disease are clinically recognizable. They were seen in two cases of familial xanthoma tendinosum. They are present to an extreme degree in patients with the nephrotic syndrome.

4. It is suggested that future attempts to relate lipids of the plasma to the deposition of lipids in tissue must take account of their combinations with protein: also, that further exploration of the protein-lipid relationships may be rewarding both in clarifying the pathogenesis of atherosclerosis and in aiding in its early recognition.

In addition to those mentioned, certain other local factors seem to play an important role in the deposition of cholesterol in the intima. Thickness of the intima seems to be very important. "Innate or acquired intimal thickening may be the most important factor in explaining why some vessels become sclerotic while others, in the same chemical environment, remain intact."[102] Increased intra-arterial pressure tends to force lipoproteins into the intima. Increased extra-arterial pressure tends to prevent excessive deposition of the lipoproteins in the intima. Vibration tends to break the protein film and precipitate the lipoids of which cholesterol is the most difficult to remove and is thereby deposited.

Duff and Payne found that the hypercholesterolemia of alloxan diabetic rabbits was not associated with as great a degree of atherosclerosis as was to be expected. In addition to hypercholesterolemia, these animals also exhibited a marked elevation of phospholipid and neutral fat.[103]

Gertler, Garn and Lerman studied lipid interrelationships in a group of 97 patients with coronary heart disease and in two control groups. They found not only a significantly elevated mean cholesterol level in the former group, but also an increase in the cholesterol : phospholipid ratio due to a disproportionate rise in cholesterol.[104]

In 1943 Hahn reported that heparin abolished alimentary lipemia in vivo, but not in vitro.[105] Weld showed that the phenomenon is not restricted to any particular vascular bed by perfusing various body regions with heparinized lipemic plasma.[106] Waldron reported that other anticoagulants (sulfinated polysacchrides and pontamine fast pink B. L.) produced effects similar to heparin. Anderson has shown that the turbidity of lipemic plasma may be cleared in vitro by mixing lipemic plasma drawn before heparinization with that formed five minutes after heparinization. He hypothesized an anti-chylomicronemic factor which results from heparin injection and discussed the possibility of a heparin-phospholipid complex being a surface active agent responsible for the clearing of lipemic plasma. Gofman and

associates found the suppression of atherosclerosis by heparin administration to be significant (the probability of no significance of this result in less than 0.01) They conclude that: (1) Heparin administered to rabbits and man causes profound reorientation in the distribution of low density liproproteins, characterized by a shift of lipoproteins of high Sf rates to those of lower Sf rates. (2) Heparin administered to cholesterol-fed rabbits prevents the development of high levels of Sf 10-50 lipoproteins and retards the development of atherosclerosis in such animals. (3) Following heparin administration the plasma contains an "active principle" associated with the ultracentrifugal globulins, which produces similar reorientation of the lipoprotein spectrum in vitro. (4) Heparin added directly to serum is ineffective in vitro. (5) Intermittent heparin administration to patients with severe angina pectoris resulted in dramatic and uniform relief from this symptom for several days beyond a single injection in 55 of 59 cases.[107]

Block, Barker, and Mann observed the effect of heparin on the alimentary lipemia which developed three hours after the fat meal. They comment that the mechanism of this peculiar action of heparin, in changing the physical state of blood lipids during alimentary lipemia, is not known. The data appear to show a true relationship between atherosclerosis and resistance to clearing of lipemic plasma by heparin.[108]

Turner and his associates have shown that in the rabbit the thyroid exercises at all times a restraining influence on the blood cholesterol, strong enough to overcome the feeding of large amounts of cholesterol by mouth. The removal of the thyroid gland resulted in rising blood cholesterol levels in normal animals and in those receiving cholesterol either with high or normal cholesterol levels at the start, the last being the so-called resistant rabbit. They also discovered that the protective action of potassium iodide depended upon the presence of the thyroid gland; and that potassium iodide failed to affect the blood cholesterol levels of the rabbit in the absence of the thyroid gland.[109, 110]

Dauber, Horlick and Katz have re-investigated the role of desiccated thyroid and potassium iodide in experimental cholesterol-induced atherosclerosis of the chicken. They conclude that desiccated thyroid minimizes the rise in the blood cholesterol level seen in the cholesterol-fed control chicken. This inhibitor effect of desiccated thyroid on the blood cholesterol was maintained throughout the course of the experiment. In potassium iodide treated chickens, the blood cholesterol levels were higher than in the cholesterol-fed control chickens. These results demonstrate clearly that when potassium iodide is given dissolved in water, with no free iodine present, it has no protective effect on the degree of the atherosclerosis induced by simultaneous cholesterol feeding. There is proof that free iodine acts peripherally by forming a thyroid hormone-like substance through combination with body proteins in areas other than the specialized tissues of the thyroid gland.[111, 112]

Stamler, *et al.* found that desiccated thyroid decreased the incidence, extent and severity of stilbestrol-induced atherosclerosis in the chick. This protective action of thyroid hormone was only partial; complete prevention of lesions was not accomplished. These findings are similar to their previous observations of the partial prophylactic effect of desiccated thyroid in chick cholesterol-induced atherosclerosis. They feel that apparently atherogenesis is promoted by any derangement of lipid metabolism inducing hyperlipemia with hypercholesterolemia and an alteration of the normal quantitative relations among the plasma lipid elements.[112, 113] The thyroid hormones influence the metabolic activity of tissues and decrease the permeability of the endothelium. Adlersburg[114] states that the common factor among most patients of young age with coronary atherosclerosis appears to be a hereditary dis-

order of lipid-metabolism manifested by hypercholesterolemia. He observed young adults with coronary atherosclerosis who were not known members of xanthoma families, but who nevertheless presented elevated serum cholesterol levels and corneal arcus. The not infrequent association of these three pathologic states, abnormally high serum cholesterol level, coronary artery disease and corneal arcus in the same individual suggested that this association might be more than coincidental. Since pathologic alteration of lipid metabolism is apparently the underlying metabolic disturbance predisposing to coronary artery disease in young members of xanthoma families, it appeared profitable to study the serum cholesterol systematically and to search for those stigmata that frequently occur in association with hypercholesterolemia. Among twenty two patients with corneal arcus and coronary artery disease, seventeen had hypercholesterolemia; among the twelve patients with xanthelasma and coronary artery disease, nine had hypercholesterolemia and among three patients with skin or tendon xanthoma and coronary arteriosclerosis, all had hypercholesterolemia. The results of this study, as well as previous observations[115, 116] and our later studies [117] support the concept that this syndrome is inherited as a dominant trait and that hypercholesteremia rather than xanthomatosis is the principal manifestation of the inherited factor. The best evidence to date that familial hypercholesteremia is transmitted as an (incomplete) dominant trait was presented recently.[118]

Our studies confirmed the postulate that hypercholesteremia represents the heterozygous abnormal state while xanthoma represents the homozygous abnormal state.[117, 119] Descent tables of thirty-five xanthoma families were presented to clarify these factors. Genetic analysis supports the concept that this disturbance of cholesterol metabolism is inherited as an incomplete dominant trait. Gene mutation produced, e. g., by exposure to ultra-violet light, may cause a metabolic change leading eventually to new growth factors. The new requirement then becomes a hereditary trait since crossing of the mutant strain with the parent strain will lead to Mendelian segregation.

Thus a single gene difference between the mutant and the parental strains produces inability to synthesize certain substances, e. g., factors of the vitamin B complex or various amino acids. Evidence is available to suggest that the mechanisms of gene action are essentially similar in all living matter, and that many metabolic pathways in man are similarly controlled by genetic factors.[120, 121, 122]

Diet Since the role of cholesterol in atherosclerosis has become more obvious and is more generally accepted, its function in the animal cell and its source in the human body has been more closely scrutinized by many investigators. According to Gubner and Ungerleider and others, cholesterol in the body derives from two sources, synthesis in the liver and ingested cholesterol in the diet. Cholesterol serves important physiologic functions as a constituent of all body tissues, as a precursor of cholic acid and steroid hormones and as a vehicle for fatty acid transfer.

Synthesis of cholesterol is chiefly carried on in the liver, the precursors being simple chemical units, such as acetic acid, as shown by deuterium tag studies.[123] Acetic acid derives from fatty acids by the mechanism of B-oxidation with removal of acetyl groups from the B-keto acids. The daily biliary excretion of cholesterol is at least 0.5 gm. and of bile acids 2 gm. The cholesterol in the bile as well as in the diet is in the free (non-esterified) form.[124]

The daily cholesterol intake in the mixed diet of the adult varies from 200 to 360 mg.; on a low fat diet it ranges from 39 to 109 mg.; whereas fat-rich diets may contain up to 1,400 mg. of cholesterol.[125] In the intestines cholesterol serves as a ma-

jor vehicle for the absorption of fatty acids, particularly the highly important unsaturated fatty acids. The mechanism whereby this occurs may be briefly described as follows: Fatty acids which are liberated by the action of pancreatic lipase on neutral fat are esterified with cholesterol by pancreatic cholesterol esterase, which is activated markedly by bile acids, in particular by cholic acid and glycocholic acid.[126, 127, 128, 129] The esterified cholesterol is transported into the epithelial cells of the intestines, unesterified cholesterol itself being absorbed poorly if at all. To be absorbed, therefore, cholesterol requires the presence of fat, pancreatic enzymes and bile salts. If any of these be lacking, cholesterol absorption is greatly impaired. Thus, in animals on a fat-free diet, cholesterol which is administered can be recovered quantitatively in the feces.[130]

Both in absorption and in transport in the blood stream (as indicated by blood concentration) there appears to be a remarkably constant concentration and division of the various lipid fractions in any individual, suggesting a dynamic interdependence and relationship. Particularly is this true for the ratios cholesterol/cholesterol esters and cholesterol/phospho-lipids. Neutral fat which usually comprises the smallest fraction of the fatty acids of the plasma is somewhat more independent and variable.[131]. The clinical significance of the close interrelationship between the various lipid fractions of plasma lies in the realization that the blood cholesteral concentrations must not be considered alone but in terms of lipid metabolism as a whole. The reason for the constancy of the partition of fatty acids between cholesterol esters and phospholipids lies in the regulatory activity of the liver in transferring fatty acids from cholesterol to phosphatides. Bloor has suggested that the constant relationship between cholesterol and phospholipid is useful to the organism in preserving colloidal equilibrium since phospholipid is hydrophilic and cholesterol is hydrophobic.[128] The hydrophobic insoluble cholesterol owes its high concentration in the serum of man to agents which allow it to be carried in colloidal dispersion.

It has been emphasized notably by Dock[102] that "where a luxus diet prevails diabetes and atherosclerosis flourish." Hence it is to be expected that high and unstable cholesterol levels will be more often found in races long used to city life, and will increase with spread of urban civilization unless effective control of atherosclerosis is developed and accepted by the populace at large.

Durant[132] has shown that the American public has increased to a very considerable extent its average consumption of fat during recent years. Comparing the per capita consumption of food for the years 1910 and 1948, he noted that there has been a significant shift toward a greater intake of fat calories, with a corresponding lessening of carbohydrate sources, the protein and total caloric intakes remaining essentially unchanged. The statistics for intervening years indicate a progressive trend in this direction. It is understandable that such a trend should occur in a land of plenty, since the culinary art has long recognized a direct relationship between the fat content of a meal and the gustatory pleasure and satiety derived therefrom. This is especially true in the dietary of a group of business and professional men considered to be average representatives of their groups. It has been well recognized that coronary disease is more prevalent in these than in the lower income groups of the country's population. Statistics for fat intake in other areas of Western civilization have indicated a very similar trend, interrupted only during the war years, when fat supplies were diverted from tables to the many and heavy demands of the god Mars, for glycerol and other fat products. Considerable evidence has accumulated to indicate that, when such reduction in utilization of fat has

occurred, there has been a corresponding decline in the incidence of coronary accidents.

Summary

In the review of the tremendous amount of literature on this subject it becomes increasingly evident that cholesterol plays the central if not the leading role in the development of atherosclerosis. It is aided and abetted by many factors, notable among which are a diet rich in fat, obesity, hormonal imbalance (hypothyroidism), an error or errors in lipid metabolism, arterial hypertension, thickening of the intima, and the aging of the intercellular fluid with alteration in its colloidal constituents. It is inhibited by many factors, notable among which are a diet poor in fats, animal and vegetable, asthenic habitus, an efficient lipid metabolism, outside pressure on the artery, a correct hormonal balance (with special reference to thyroid and pancreas), heparin and heparin-like substances.

Much attention has been called to the differences inherent in various species of laboratory animals and in man in the ability to metabolize unusual quantities of fat in the diet. The differences in ability to metabolize a diet rich in fat and cholesterol content among members of the same species has not received the emphasis the facts would appear to justify. Wilkinson and Adlersberg in their work on familial hypercholesteremia and the inborn error of lipid metabolism have pointed the way for further and much more extensive investigation. They have pointed out along with Durant that what is obviously needed is a long term, well controlled clinical study.

The observant clinician, in the study of his patients over a period of years, becomes increasingly aware of the fact that there are certain families whose members can tolerate diets rich in fat and cholesterol, whereas members of certain other families cannot. The study should include several generations. As an example, I have in mind one family which has been under very close observation for many years. There are many members now in the fourth generation. The first two generations were country folk, who sold most of their butter and eggs for pin money; who rendered all their animal fat into lard and tallow. Mayonnaise and rich gravies were unknown to them. The four generations comprise approximately 100 persons among whom there has not been a single case of obesity and the only known coronary attack occurred in a 79-year-old male. Many clinicians with careful family histories can accumulate evidence that will be of material aid in determining the prevalence of this inborn error.

The life history of the individual tends to recapitulate the life history of his family. The individual member of a family who has thus become accustomed to an elevated lipid and cholesterol content of the blood plasma can, and apparently does, maintain that level by synthesis on a low fat and cholesterol diet. However, since this error must be present in the general populace, in varying degrees of severity, rigid restriction of cholesterol and fats, animal and vegetable, may hold some promise of success in the prevention of atherosclerosis among those people who have the inborn error to a lesser degree. Durant is of the opinion that if an appreciable reduction in blood cholesterol is obtained and maintained with due regard for the usual fluctuation in level observed in atherosclerotic individuals, it is probable that a definitely beneficial effect is being obtained. The results obtained by the use of thyroid extract, heparin and heparin-like substances hold some promise that research may provide a means of attacking the disturbed lipid metabolism of atherosclerotic patients in such a manner that they may safely enjoy a liberal fat intake.

The evidence to date makes reasonable the hypothesis that the "luxus diet" mentioned by Dock and others may be the error which serves as the predominant etiological factor in the development of inborn errors in lipid metabolism in subsequent generations.

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212 Huntington Street, East

New Drug for Treatment of Certain Types of Epilepsy

A new anticonvulsant drug — hibicon (trade mark)—has proved effective in the treatment of grand mal and psychomotor epilepsy, it was reported in the *Archives of Neurology* and *Psychiatry*, published by the A.M.A.

A compound differing in chemical nature from other modern anticonvulsant drugs, hibicon has been found singularly free from toxic reactions and from untoward side-effects, according to Dr. C. D. Hawkes, of the department of neurology, University of Tennessee College of Medicine, Memphis.

"In 23 of the 39 patients whose seizures were satisfactorily controlled by hibicon, the results were rated as excellent," Dr. Hawkes pointed out. "These patients were seizure-free or had only rare attacks. In 16 patients, the control was rated as good; these patients had one to four attacks a month, but were nevertheless greatly benefited.

"In the remaining 20 patients placed upon hibicon therapy during the two-year trial period, the compound failed to hold the attacks below one a week, and the result was classified as poor. It is only fair to state that in eight of these patients the seizures have never been adequately controlled by any anticonvulsant drug or combination of drugs.

"The employment of hibicon appears to widen the scope of the pharmacological therapy of chronic epilepsy, since it has successfully controlled the seizures in some patients whose attacks have failed to respond to all other present-day anticonvulsant drugs."

According to Dr. Hawkes, hibicon also was found to be beneficial in the treatment of mixed forms of epilepsy upon the addition of small amounts of barbiturates, and has been proved effective in the treatment of idiopathic and symptomatic epilepsy. Petit mal epilepsy, he added, is not benefited by the drug.

Hibicon is a white crystalline solid which has a low solubility in water, but is readily absorbed after oral administration, Dr. Hawkes stated. It has a wide safety margin, and side-reactions are uncommon and usually minor. The effective range of the adult dose appears to be from one to two grams three or four times a day. In small children, a dosage of one-fourth to one-half gram three or four times a day has been found satisfactory.

Bladder Dysfunction in Children Due to Congenital Defects

Bladder Neck Obstruction and Neurogenic Bladder

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Alertness on the part of the general practitioner and pediatrician in recognizing the signs and symptoms of bladder dysfunction in a child or infant is the only hope for an early diagnosis in patients with congenital bladder neck obstruction and neurogenic bladder. Early diagnosis means much to these patients as severe and irreversible changes in the upper urinary tract may develop in a short period of time, damage sometimes having already occurred at birth.

Difficult frequent urination, straining to pass only a few drops of urine, dribbling, recurrent pyuria and pus in a small boy's urine are signs which should not be passed upon casually. Some of these patients are wet constantly and tend to drip urine, instead of emptying the bladder at normal intervals. The same pattern may be more marked at night, but the functional bed wetter voids at intervals even though he is asleep.

In congenital bladder neck obstruction the alteration in the mechanism of micturition in the child is much the same as in prostatism in the elderly man. The detrusor not being able to overcome the increased resistance at the bladder neck results in a dilated bladder, trabeculation in the bladder wall and ultimately dilatation of the ureters and hydronephrotic kidneys. Differentiation between bladder neck obstruction and neurogenic bladder may be difficult as the signs may be similar. The basic pathology is different, but the alteration in the mechanism of voiding is much the same.

In the latter the resistance at the bladder neck is normal but the detrusor is weak, due to inadequate nerve supply; consequently, unable to overcome the resistance of the normal bladder neck, inability to properly empty the bladder results.

Differential diagnosis and treatment of these two conditions is a job for the skilled urologist, but the general practitioner can screen these patients with relative ease. Immediately, after the patient voids, catheterization will determine the amount of residual urine present. If more than a few cc. are found remaining in the bladder, one would suspect that there is difficulty in emptying and further investigation is in order. A flat film of

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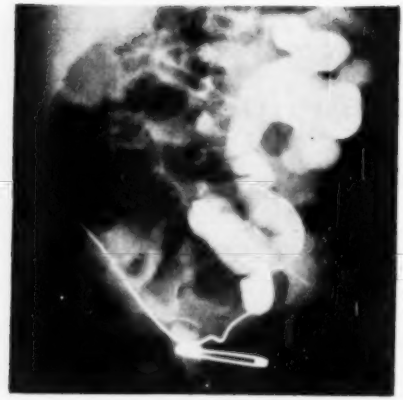






Fig. 1

Illustrations showing the necessity of surgery on the upper as well as the lower urinary tract in an 18 month-old boy.

A (top) Enormously dilated left ureter before surgery.

B (center) Following relief of bladder neck obstruction (retropubic) and pyelostomy left, a large redundant ureter remains making it impossible to clear up infections.

C (bottom) Result after partial ureterectomy (mid portion) and intubation.

the urinary tract and pelvis may show a defect in the sacrum which would suggest the possibility of a neurogenic bladder. Before treatment is planned an accurate diagnosis and evaluation of the urinary tract should be made. A cystogram, filling the bladder to capacity by gravity, may show reflux up both ureters in cases where severe damage has taken place. Intravenous urograms may be helpful if the renal function is adequate to excrete the media and in either case, a test of renal function should be made. Cystoscopy, retrograde pyelogram, etc., may be necessary and blood studies such as N.P.N., etc., are essential. The general condition of the child is also important. Malnutrition is often the most outward expression of chronic renal disease and, in long standing cases, dwarfing may result from renal rickets.

Medical treatment of recurrent attacks of pyuria in a child without evaluation of the urinary tract is unforgivable. If either of the above conditions is present, surgery directed to the bladder neck by transurethal resection or by the retropubic route may cure or arrest the condition. If the ureters remain dilated after the bladder neck obstruction is relieved or obstructions are present in the upper urinary tract, further surgery in this area may be necessary.

A surgeon who operates on the bladder neck obstruction and fails to follow the changes in the upper urinary tract may be lulling himself into a false sense of security.



Fig. 2. Pyelogram of left side, 3-year-old boy showing dilatation of kidney and ureter resulting from congenital bladder neck obstruction. (Permission **Southern Medical Journal**)[1]



Fig. 3. Intravenous Urogram of 3-year-old boy. Note defect in the sacrum suggesting neurogenic defect causing dysfunction of the bladder and dilatation of the upper urinary tract.

Summary

In spite of the rather discouraging picture that these patients may present many of them respond well to treatment. The screening of these patients lies first with the family physician or pediatrician, who, if he recognizes the condition early, deserves the most credit for their salvage.

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406 University Hospital

A New Long-Acting Androgen, Testosterone Cyclopentylpropionate

The duration and degree of response of the new androgen, testosterone cyclopentylpropionate (TCP), was compared with that obtained with testosterone propionate by subcutaneous injection of 5 mg. of each compound into young intact and castrated male rats. In castrated rats the duration and response of the seminal vesicle and prostate effect was greater and of longer duration with TCP than with testosterone propionate. By the 30th day the effect of TCP was 10 times that of the propionate. It required 25 mg. of testosterone propionate to give comparable results to 5 mg. of TCP.

According to Ott *et al.* in *J. Clin. Endocrinol. Metabol.* [*12*:15 (1952)], it was found that a single injection of TCP was able to stimulate the seminal vesicle and prostate growth in castrated rats so that by the 18th day the response was practically equal to the growth expected from the animal's own testicular secretion.

The Principles of Electrosurgery for the Removal of Superficial Skin Tumors

The present day usage of the term electrosurgery is restricted to the application of high frequency currents to generate heat in tissues, causing cell destruction. By high frequency current we understand an alternating current having oscillations of a million or over per second.

The prerequisite for the safe and efficient application of electrosurgery is that the physician should have a working knowledge of electrophysics, and a familiarity with the instrument. The physician must also acquire practical experience in the employment of the various currents, so that he may be constantly aware of the physical process that transpires in the apparatus, so that he may understand the physical effect of the current which emanates from the different electrodes upon the various tissues, and so that he can predict the physiological consequences of the physical effects in those tissues.

While physicians are not equipped and should not attempt to repair a breakdown in the apparatus they must be able to distinguish at once whether a breakdown is in the apparatus or a minor trouble exists, such as a loose set screw to the control dial, a blown out house line fuse, a loose connection, or a broken cord or socket. These latter disorders he should be able to repair. The familiarity with and authoritative usage of the instrument tends to reassure apprehensive patients, who might otherwise not submit to treatment.

A physician equipped with the necessary knowledge and the skill can utilize with great convenience the method of electrosurgery in a large number of minor surgical conditions and can obtain excellent results with a safe but simple and inexpensive equipment in his office where with other methods the results might not be satisfactory.

PHYSICAL PRINCIPLES OF THE HIGH FREQUENCY APPARATUS

The Power Source At present the usual power source is the 110 V 60 cycle alternating current and all apparatus is constructed to accommodate this current. To use them for other currents the power source has to be transformed to the mentioned current.

Alternating current is one which flows for a period of time in one direction and then for an equal period of time in the opposite direction. In this period the alternating current undergoes changes and completes a cycle from zero voltage to zero voltage with a peak in the positive phase and with a peak in the negative phase. The 110 V 60 cycle alternating current is one which has a tension at its peak of 110 V and has 120 alternations to complete 60 cycles in a second (Fig. 1). The source of the electric current has no relation to the tissue response to the high frequency current.

A great variety of reliable surgical diathermy apparatus is available, therefore it would be impractical to discuss the working mechanism of all of them. A simple but safe and efficient apparatus for office surgery has been selected to be

used as basis for the explanation of the working principle of a spark gap surgical diathermy.

The Power Circuit The 110 V 60 cycle house current has to be altered in two ways to generate sufficiently high frequency current with enough power to produce adequate heat for tissue destruction. 1. The 110 V tension has to be stepped up to a couple of thousand volts. (This is done with a transformer.) 2. The 60 cycles have to be increased to 1 to 2 millions of oscillations per second. (This is attained with a spark gap.)

The transformer consists of two copper coils completely insulated from each other, which are wound around a laminated sheet iron core. One coil, the primary, consists of several hundred turns, the other, the secondary, consists of several thousands of turns of a much thinner wire. When the alternating house current flows through the primary coil it induces electricity in the completely insulated and in no way connected secondary coil by electromagnetic force. The voltage of the induced current will depend on the voltage supplied to the pri-

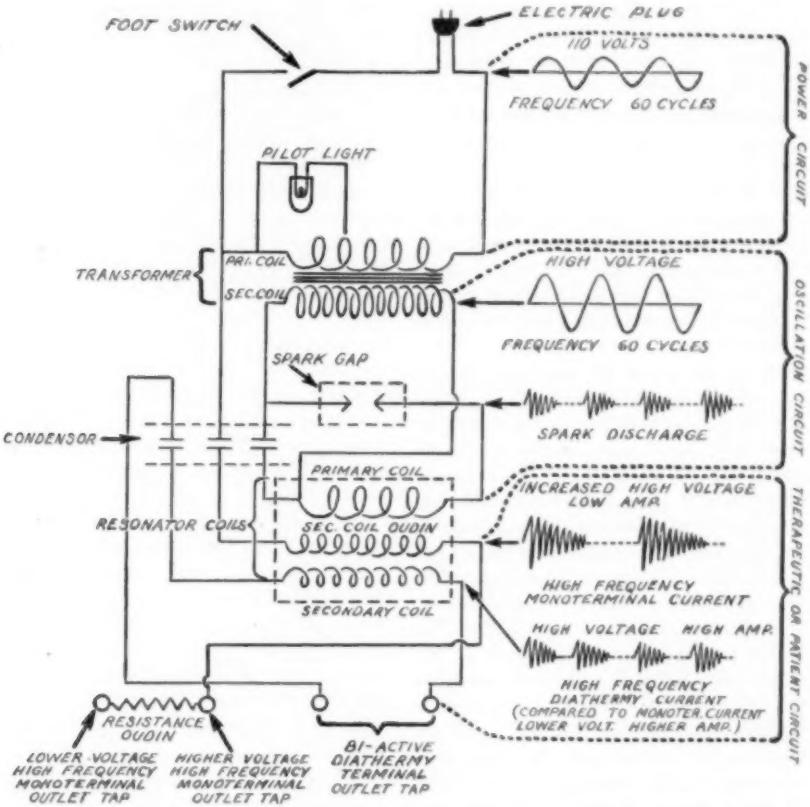


Fig. 1. Wiring diagram of a spark gap surgical diathermy apparatus, showing schematically the changes which have to be affected in the house current to produce the high frequency and high voltage current used for desiccation and coagulation.

mary coil and on the ratio of the number of turns between the primary and secondary coil; in other words, if the secondary coil has a hundred times more turns than the primary, the current flowing from the secondary coil will have a hundred times higher voltage.

The size of the wires used in the two coils will determine the capacity of the output in the apparatus. A current to be usable for electrosurgery must have a comparatively large volume (amperage) in order to have adequate power for tissue destruction, while the height of the tension will regulate the penetrating power, which in electrosurgery can be relatively lower than that in medical diathermy, as the penetration necessary is usually a fraction of an inch. (Fig. 1)

Oscillation Circuit or Generator Circuit The current with tension increased to several thousand volts flows from the secondary coil to the capacitators and charges them. When the capacitators reach a sufficiently high tension they will discharge through the spark gap and then the current will flow through an inductance coil, which is also called a resonance coil.

The discharge of the condenser across a spark gap produces an oscillating current of unequal voltage as the voltage diminishes with each subsequent oscillation until it reaches zero. The oscillations which appear in wave trains of diminishing voltage are called damped wave oscillations. After each oscillation period there is a rest period during which the capacitators become charged anew. The wider the spark gap the higher will be the tension which accumulates in the capacitators before it will break down the gap and discharge across it, therefore with a wider spark gap the rest period will be longer. The distance of the spark gap according to the aforementioned will regulate the tension (voltage) and the current intervals (damping). The spark frequency can be varied but the frequency of the oscillations of the current during each period remains constant. The rate at which the current oscillates depends only on the inductance of the resonator coil and upon the capacity of the condenser, which are constant, thus the wave length or frequency at which the apparatus works cannot be changed by the adjustment of any dial. The oscillation frequency is invariable in a given apparatus. Spark gap electrosurgery apparatus is designed to work at frequencies between 1 to 2 million, i. e., it emits radiation of a wave length of 300 meters and below. (Fig. 1)

The Therapeutic or Patient Circuit The oscillations produced in the generator circuit are transferred through the resonator coil to the therapeutic circuit, which consists of a resonator coil and a capacitator, capable of responding to oscillations of the same frequency as the generator circuit produces. The condenser in the therapeutic circuit functions also as a safety device against grounding the patient with high tension current should a breakdown in the apparatus occur, as the high frequency current passes through the dielectric plates of the condenser, for they do not offer any resistance to the high frequencies, but their resistance to low frequency current is so great that they act as insulators and no low frequency current passes through them.

The spark gap apparatus has in the therapeutic circuit another resonator coil consisting of turns of a very fine wire, which steps up the voltage so high that current will flow from a pointed terminal of an electrode to the patient without the patient being connected to the other terminal of the apparatus. This coil is known as the monoterminal or Oudin coil. (Fig. 1)

The Effect of High Frequency Current The physical effect of a high frequency alternating current which passes through the body is production of

heat, which is in direct relation to the strength and duration of the current and in relation to the resistance encountered by the current in the various tissues. The basic factor in all electrosurgical methods is the increasing of the density of the current under a small electrode so that the concentration of the current will result in generation of intense heat causing desiccation, coagulation or explosion of the cells while during this process the electrode remains cool. The amount of current needed for the various procedures will vary according to the resistance encountered. Observation of the actual coagulation produced by the electrode and not ampere meters will guide the operator in regulating the current strength to achieve the desired results. A monoterminal current has no meter and the sudden and violent fluctuations of the biterminal current, which might damage the meter, makes its application inadvisable.



Fig. 2
Electrodesiccation of a skin tumor using a footswitch equipped apparatus to safeguard the operator from "shock" due to current leakage.

The Technique of Application

Before treatment the operator should ascertain himself that all connections are proper and firmly attached, that the cords have no breaks or worn spots and that the apparatus is in good working order. The patient is situated according to the part to be treated on a non-conducting table. A wood table with dimension of 32″ x 18″ x 66″ is suitable for the majority of procedures. Since the high frequency current, which flows from the electrode to the patient, will build up a static charge on the patient's skin surface, resulting in a spark discharge, if the patient touches a metallic object, metal tables for treatment can be used with the following precautions:

1. The patient should hold on with firm grip to the exposed metal of the table; or a metal armband should be placed around the patient's wrist and the armband should be connected through a chain with the table. This arrangement does not permit the accumulation of electric tension on the patient, as the electricity will be drained away as rapidly as it is produced and therefore no voltage difference can arise between table and patient.

2. The operator may place his left hand on the bare skin of the patient and thereby draw away the current through his hand and body to the ground. (Fig. 2) In this latter case the operator acts as a ground connection to prevent the accumulation of

potential difference between patient and ground and the patient will not experience a "shock" when he touches ground.

Electrodesiccation (Fig. 2). The monoterminal comparatively high voltage and low amperage current is discharged from the Oudin terminal of the diathermy apparatus through the needle point electrode which is held in contact with the lesion or at a slight distance from it and will cause desiccation of the tissues through evaporation of water. Fig. 3a, b) For best results the strength of the current should be held low and applied for only a short period, never longer than 2 seconds. While the current is on, the electrode should be glided over the tissue, but it should never be lifted off of the tissue, as this causes sparking. By this method the discomfort to the patient can be kept to a minimum and the majority of superficial growths can be removed with little pain, making it unnecessary to apply anesthesia. The keratin cells of some warts are very poor conductors and if one should apply the electrode to the surface of the lesion the current would pass to and concentrate in the surroundings of the growth and would cause blistering of the adjacent skin, while the growth center of the wart would remain undisturbed. In these cases it is necessary to insert the needle deeply to the soft base of the wart. The intensity of current necessary for the desiccation of these warts will be directly proportional with the diameter of the needle and with the depth of its insertion. (Fig. 3c)

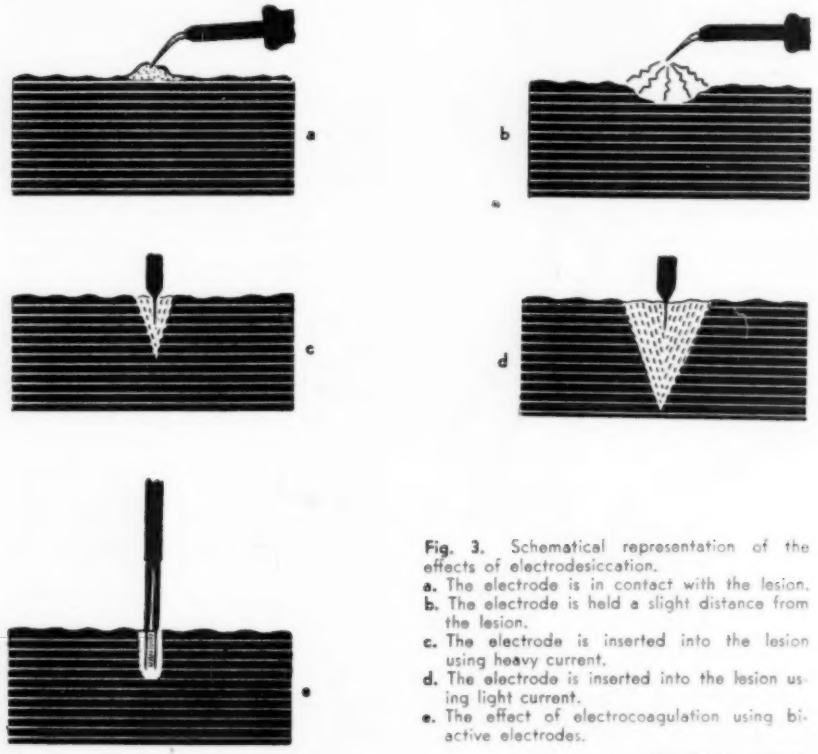


Fig. 3. Schematical representation of the effects of electrodesiccation.
a. The electrode is in contact with the lesion.
b. The electrode is held a slight distance from the lesion.
c. The electrode is inserted into the lesion using heavy current.
d. The electrode is inserted into the lesion using light current.
e. The effect of electrocoagulation using bi-active electrodes.

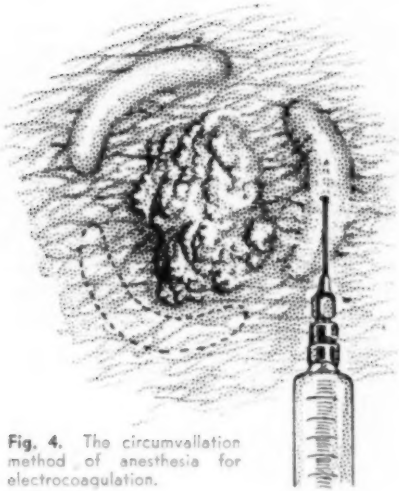


Fig. 4. The circumvallation method of anesthesia for electrocoagulation.

The desiccation is completed when the spark lights up the entire lesion and the lesion turns white. The best cosmetic results are obtained when the desiccated tissue can be left in place until it separates and falls off, which occurs usually within 10 days. If the lesion has to be curetted the remaining crater should be lightly sparked over to prevent bleeding. In most cases no dressing is necessary.

The monoterminal discharge from the Oudin terminal is difficult to insulate and has the tendency to leak off from the conductor cord to the operator's hand or to the ground if the electrode is lifted off the patient when using electrodes with make and break contact on the handle. To eliminate this leakage a foot control is essential.

Electrocoagulation with Bi-active Electrodes For the destruction of larger lesions electrocoagulation is the procedure of choice. For electrocoagulation local anesthesia is necessary. Two per cent Novocain should be injected around the lesion or regional anesthesia should be used. (Fig. 4)

The current necessary for this type of work is of relatively lower voltage and higher amperage. The electrode consists of two insulated needles which are mounted parallel to each other in one handle and which are connected separately to the terminals of the apparatus. Both electrodes concentrate the current and the current flows only between and around the needles. (Fig. 3e)

For the application of this method it is necessary to note that heavy current applied for a short period of time will coagulate a lesser amount of tissue than current of lesser power applied for a longer period of time, because the heavy current will dry out the tissue and the dry tissue offers a resistance to the current, while the lighter current permits the tissues to retain their fluids for a longer period of time and thereby the current has an opportunity to penetrate farther. (Fig. 3c, d)

Excess current might lead to arcing between the two electrodes and thereby to burning out of the electrodes.

Upon completion of the coagulation a dressing should be applied. Antiseptic and granulation-promoting salves can be applied upon the lesion. The healing will take place within 10 days to one month according to the size of the lesion removed.

EDITORIALS

Future of the American Academy of General Practice

Behold, there came up the champion, Goliath by name, out of the armies of the Philistines—I. *Samuel*, xvii.

The managing publisher of GP, Mr. Mac F. Cahal, who seems to dominate the editorial section of the journal of the American Academy of General Practice every month, comments peevishly in the August issue on an editorial we published in December, 1951 ("Future of the American Academy of General Practice"). In quoting us to the effect that the editors of GP should be general practitioners and that only articles written by general practitioners should be accepted for publication, Mr. Cahal says "a small medical publication" made these recommendations. It was we who made the criticisms in question. We said a good deal more regarding the dubious future of the Academy if it continues to utilize the talents of specialists almost if not quite exclusively in its GP columns and in its assemblies. We postulated a future Academy, naturally enough, which would logically utilize talented general practitioners almost if not quite exclusively.

Mr. Cahal contends, in his querulous August editorial, that GP can't get all the good articles it wants or needs, despite the fact that as a "non-profit institution" GP can afford to put its money into subsidies to writers since it does not have the responsibility of private enterprises like the publishers of the MEDICAL TIMES of paying taxes and helping to support American economy. We leave the members of the Academy to cogitate upon the following remarks: "We want only the best—preferably by general practitioners. But we won't sacrifice the best just to have general practitioners do the writing." The same fair-seeming policy governs the assemblies.

Yet we do not charge a boycott of general practitioners. The spectacle is merely good fun and we are only laughing.

Since Mr. Cahal has introduced the topic of a medical journal's avoirdupois, characterizing us contemptuously as "a small publication," we feel no chargrin in admitting the vast superiority in size and weight, which seem to determine excellence in Mr. Cahal's code, of his beloved GP, a very Goliath in poundage in the armies of journalistic Philistines.

Our interest in the future of the American Academy of General Practice and in its recapture is sincere. What in thunder led to its creation other than the promotion of the total interests of the general practitioner—by far the most glamorous figure in the Pantheon of Medicine? To the degree that those interests are safeguarded or jeopardized will depend the triumph or eclipse of this very great figure and of his nobly conceived Academy.

A. C. J.

Planning the "Cradle-to-the-Grave" Nightmare

It can no longer be denied by the political charlatans of Washington that the government now in their power is being steered toward socialism, for they now openly advocate federal sharing in the costs of adult and family welfare services

and insist that this should be done in behalf of *all* who wish such services, *regardless of their financial need.*

Visualize the "national health insurance" these charlatans are hell-bent on submitting to the new Congress, with no distinction between rich and poor beneficiaries. Who is so brazen today as to deny that this system in operation would be, not just an entering wedge, but an actual phase of socialism?

Until recent avowals of the true goal the taint of socialism has been denied.

Rat Race

Further increase in world population will increase the pressure for food and there is a shortage of arable land. The world population increase proceeds at the rate of 20,000,000 a year. In the old days crude adjustment was accomplished through pestilences and wars. Only wars remain but they are not adequate as presently conducted. Lack of biologic methods of contraception applicable to masses, whether such masses are intelligent or not, rules out this now undependable resource, and in any case paternalism is conserving millions of consumers. With increasing crime the prisons and jails provide additional non-productive consumers.

The obvious answer is atomic war, which will exterminate peoples on an unprecedented scale. In the present trigger state of a world in the power of uncouth, inept and corrupt politicians, and with intensive production of atomic weapons and hydrogen bombs, the "danger" will be wars that will be much more than adequate.

What a rat race!

Health Needs of the Nation

Labor has submitted some interesting facts and opinions to the President's Commission on the Health Needs of the Nation. It sees the mounting cost of living tending to cancel out the protection afforded by such aids as the Blue Cross, the Blue Shield, and the indemnity programs of one sort or another. Labor, it appears, while seeing mounting costs making sickness a luxury, does not want political medicine. Dr. Gilson Colby Engel, president of the Pennsylvania Health Council and professor of clinical surgery at the University of Pennsylvania, advised the Commission to see that Mr. Ewing's Federal Security Agency be shorn of its health services. This would involve the creation of a new health administration headed by a Secretary of Health with Cabinet status.

If the political control of health can be ended the nation's health record—death rate cut almost in half between 1900 and 1950—will be still further improved.

The Soviet Population Trend

According to the Population Reference Bureau of Washington, D. C., the Soviet Union has achieved a low birth and death pattern. This has been done at a fast rate (35 years) compared with the record of the Western nations (100 years) and may be taken as an index of phenomenal improvements in medicine and technology.

The Bureau has reason to believe that the Kremlin is not pleased with the falling birth rate, which does not jibe with its plans for the enslaved masses.

The Soviet population is estimated at 207,000,000 with a yearly increase of 3,000,000. This increase has shown a continual decline since 1935.

As in the United States, the Soviet population is shifting from rural to urban areas.

PUBLIC RELATIONS

Weintrob on Bernays

PUBLIC RELATIONS, by Edward J. Bernays, 374 pages, Norman, Oklahoma, University of Oklahoma Press, $5.00.

This book by Bernays, formerly Professor of Public Relations at New York University and the University of Hawaii and frequently referred to as the founder of the profession of Public Relations, contains but slight reference to the "P. R." problems of American Medicine *per se*. Nevertheless, the subject matter is so well presented, making use of the case-example technic, that its lessons are applicable to medicine and should be learned by every doctor in the U. S. A.

The all-too-frequent so-called "book review," thrown together hastily from the publisher's blurb on a book's jacket, in this instance, as in most, would be a waste of journal space and of little value to serious students. To do justice to Bernay's well-organized presentation would require several printed pages.

An old "P. R." man once said, "Good Public Relations is simply this: 'Do right and let people know about it.'"

Bernays points out that "things and ideas compete for public interest and support, to fasten people to existing beliefs and actions, to convert or negate them. The Bill of Rights by implication endorses competition as an essential part of our democracy in the field of ideas for it guarantees us freedom of speech, press, petition, assembly, and religion—all of which encourage the *principle of freedom of choice*. In totalitarian regimes competition does not exist. Government control enforces both a monopoly of ideas and things."

American medicine can learn several fundamental lessons from Bernays' book:

"The needs of our society demand competition, but the interest of a group should not, in its competitive striving, be permitted to run counter, as sometimes happens, to society as a whole."

"Public relations facilitates adjustment and accommodation to the times. Men and institutions often lag behind contemporary public opinion. The objective-minded 'P. R.' man helps his client adjust to the contemporary situation or helps the public adjust to it."

It was Charles Merriam, of the University of Chicago, who said, "The difference between evolution and revolution is the rate of change."

To which Bernays adds: "The great reliance on publicity as such is striking and significant. Modern psychology teaches us that information usually acts merely as an intensifier or weakener of preconceived attitudes and has very little part in the process of persuasion."

Yes, "the public be damned" attitude has given way to "the public be informed" approach. This was recognized in 1922 by Col. Robert Stewart, Chairman of the board of directors of the Standard Oil Company of Indiana, when he said:

"It is not enough to advertise a product. Public opinion ought to be acquainted with the honesty and high character of the institution back of the product. I have always believed that one of the biggest jobs of the head of a business is to undertake definitely to deserve favorable public opinion and then to go out and win it."

How can good Public Relations counsel help American medicine overcome the present "bad press," the attitude of the people which is expressed in the phrase, "my doctor's all right but the American Medical Association is reactionary and unwilling to change with the times"?

As Bernays remarks, "in the flux of a democratic society there are maladjustments between individuals and groups, on the one hand, and society as a whole or sections of it on the other."

This is directly applicable to organized medicine's problems as it seeks to "sell itself" to the various ethnic, financial, social, cultural and other segments of the public

It is good public relations to note the American's desire to "show me the facts" . . . to demand "let's take a look at the record." This technic for selling free enterprise in medicine is essential. But, good public relations procedure also takes into account the role that tradition takes in our culture and, since we are dealing with human beings, the great part emotion plays.

Though Americans are nationalistic, they are strongly individualistic. Hence, public opinion cannot be compelled since compulsion is contrary to our traditions of freedom and equality. Many Americans resent the effort of "government" to do their thinking for them for, after all, "government" is made up of human beings, too frequently, alas, no brighter than many private citizens and, too often, subject to human foibles which lead to actions causing public distrust in the ways of government!

Perhaps that is the fundamental reason why Messrs. Truman and Ewing's so-called National Health Insurance plan, which is actually socialized medicine, is unpalatable except to a vociferous minority of do-gooders, outright socializers and misguided trade-unionists whose leaders favor the program because of misinformation and inability to foresee what harm it will eventually bring to labor.

All sorts of dire threats have subtly and even overtly emanated from the White House and the Federal Security Administration; but as was said by Winston Churchill in his World War II Memoirs; "It is easier to infuriate Americans than to cow them."

American medicine needs the best public relations obtainable and it cannot take time out to rest. Defeated in their frontal attack, the "do-gooders" seek success by the back-door technic and piecemeal passage of bills tending to increase bureaucratic control over our way of life. They are experts in the old Roman technic of "divide and conquer."

To keep American medicine in the realm of free enterprise, we need the wholehearted support of an enlightened public opinion and we must be prepared to pay the cost of a long-range program that knows no holidays.

We dare not oversimplify the problem, stressing what the opposition calls the shibboleths of "the American Way" and "Free Enterprise." Two decades of basking in governmental favor have given a new meaning to "the American Way of Life" to trade unionists who now make up a sizeable and powerful segment of the public. Though trade-wise pressure on management can hardly be called "free bargaining," unions include this in their definition of "free enterprise." What the "fringe benefits" obtained by this method have done to narrow "free enterprise" in medicine should be evident to every thinking physician with even an elementary knowledge of medical economics!

Nevertheless, we must guide ourselves by events and by the thinking of those who lead the public we hope to continue to serve as doctors. Can medicine's public relations overlook the following statement by Walter Reuther, who speaks for one million American unionists who, with their families, make up 5 million in all?

"We are still far from the goal we seek. Insecurity still haunts millions. Inadequate housing poisons the wells of family life in vast numbers of cases. Inadequate schooling handicaps a good segment of our people and the fear of sickness and old age still clutches the hearts of many, if not most, of our fellow citizens. Until we solve all these problems, and quiet all these fears, our people will not be truly free."

This reviewer is unalterably opposed to Compulsory National Health Insurance and

was an active speaker representing the Kings County and New York State Medical Societies in debates against those who sought to effectuate socialized medicine. But, he feels it wholly inadequate to counteract remarks such as those made by the above-quoted, highly influential trade-union leader (a member of the President's Committee which is supposedly unbiasedly examining the present state of our nation's health) by holding aloft the time-honored banners of "Free Enterprise" and "The American Way of Life."

The public wants and will get more than our prepayment, voluntary health insurance plans now provide. Good public relations counsel, even though it may cost us plenty, must determine *what* is wanted, *whether* and *how* it can be done, and *must guide us in the troubled years ahead*. American medicine is at the crossroads in a world giving every evidence of a swing to the left.

Social-minded, self-enlightened, well-informed public relations can do much to keep us on the correct road. Books like those by Bernays are helpful in orienting both our thinking and our actions.

Although this reviewer considers Bernays' book one each doctor should read, it is not to be inferred that the author sees eye to eye with the vast majority of American physicians. In fact, Bernays seems to have little, if any, faith that voluntary prepaid health insurance plans are the answer.

In a personal communication to this reviewer he stated:

"I am afraid that you are in error in deducing that I am opposed to the Ewing-Truman Nationalized Compulsory Health Insurance Plan. Over the years we have had a great deal of experience and practice in the public relationships of health. Many years ago we advised the Committee on the Cost of Medical Care on their public relations, and that experience brought me closely in touch with the needs of the American people for proper medical care and the impossibility of securing it through ordinary channels. It is my reasoned conclusion that one of the ways to preserve our American system and the democratic way is to ensure that everyone has the opportunity to receive adequate medical care.

"It is my further belief that the quickest method of securing this is along lines of plans that have been effectively worked out in England and in other countries."

With which conclusions this reviewer cannot agree because the weight of evidence, we are convinced, points the other way. However, Bernays is a seasoned investigator and, doubtlessly, like some others who think as he does, honestly convinced of the rightness of his beliefs. American medicine cannot class all opposed to the "voluntary method" as being "misguided do-gooders." Name calling will not solve the problems. Good public relations will help. Among the problems facing American Medicine in its fight to keep government from lowering standards of medical care as it has done "in England and other countries" is to *show the facts* to men of the high caliber of Bernays and others like him in the hope of convincing them that *Socialized Medicine would rob both the health and the pocketbook of the American public.*

Morris Weintrob, M.D.

MEDICINE

MALFORD W. THEWLIS, M.D.*

The Effect of Penicillin on the Renal Lesions of Subacute Bacterial Endocarditis

D. M. Spain and D. W. King *(Annals of Internal Medicine*, 36, 1086, April 1952) report an autopsy study of 77 cases of subacute bacterial endocarditis, in 25 of which penicillin therapy had been employed. In the untreated cases, 33 per cent showed diffuse glomerulonephritis. In an earlier study of a larger series of untreated cases of subacute bacterial endocarditis, the incidence of diffuse glomerulonephritis had been found to be 29.5 per cent. But none of the treated cases in the present series showed evidence of diffuse glomerulonephritis. Six, or 24 per cent of these treated cases, showed focal embolic glomerulonephritis, while 25, or 48 per cent of the untreated cases, showed this complication. In the treated cases, the penicillin treatment was begun on the average within one and one-half to two months after the onset of symptoms of subacute bacterial endocarditis; it is possible that this early institution of treatment was of importance in the elimination of the renal lesions. There was no significant difference in the age of the patients, the duration of the disease, or in the underlying cardiovascular disease in the two groups (treated and untreated cases). In the 25 treated cases, the valvular vegetations were found to be active with little if any evidence of healing in only 4 cases, in 10 cases the lesions showed a considerable degree of healing, and in 11 cases appeared to be completely healed. Death in these cases was due to congestive heart failure in 10 instances and to the consequences of "embolic episodes" in the other 15 cases; 7 showed ruptured valve cusps. In none of these cases was death due to renal insufficiency. In the untreated cases death was due to uremia in 9 cases. The fact that the elimination of the infecting organism by antibiotic therapy prevents the development of diffuse glomerulonephritis in subacute bacterial endocarditis, indicates that this is a different disease from diffuse glomerulonephritis not associated with subacute bacterial endocarditis, in which the lesion progresses even if the infecting organism does not persist.



Thewlis

COMMENT

This last sentence sums up the important point. M.W.T.

The Use of Mercurial Diuretics in the Treatment of Bromide Intoxication

A. E. Hussah and H. L. Holley *(American Journal of Medical Sciences*, 233:262, March 1952) report the use of the mercurial diuretic mercuhydrin in 3 cases of

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bromide intoxication. In 2 of these cases, sodium chloride was also given, and in one case, ammonium chloride. When the two agents were used together, i.e., sodium or ammonium chloride and mercuhydrin, the effect was "additive." The mercuhydrin increased both the volume of the urine and the concentration of bromide in the urine. The chief indication in the treatment of bromide intoxication is the rapid elimination of bromide from the body fluids. Mercuhydrin used with the chlorides is of definite value in this respect: it prevents any increase in the level of the blood bromide which might result from the administration of large amounts of chloride, by inducing rapid elimination of the bromide by the kidney, thus clearing the toxic drug from the blood stream promptly. These findings indicate that the combination of a mercurial diuretic with ammonium or sodium chloride is the most effective treatment for bromide intoxication.

COMMENT

Ensures an effective, rapid elimination of bromide. Bromide poisoning is rather common and should always be kept in mind. I seldom see it in my patients—perhaps because I seldom use over 5 grains for each dose. Like many other drugs which cause toxic symptoms, if they were used in smaller quantities there would be fewer toxic effects. For forty years I have used bromides in 5 grain doses; I have checked the blood frequently for poisoning, but so far have never seen any ill effects from this amount. And the therapeutic effects have been satisfactory. There is a tendency today to use too large dosage of many drugs. For example, five grains of aspirin will usually be as effective as 15 grains.

M.W.T.

The Thiouracil Drugs in the Treatment of Chronic Ulcerative Colitis

R. A. Herfort and H. H. Livingston (*New York State Journal of Medicine*, 52:431, Feb. 15, 1952) report 15 cases of chronic ulcerative colitis treated with thiouracil and propylthiouracil, thiouracil being used in 8 cases and propylthiouracil in 7 cases. Thiouracil was given in a dosage of 200 mg. three times daily and propylthiouracil in a dosage of 100 mg. three times daily. In each case, the drug was employed for at least three months and was continued until there was significant improvement in symptoms. Of the 15 patients 8 were females and 7 were males; the ages ranged from eleven to fifty-two years, and the duration of the disease from six months to fifteen years; in all but 2 patients the onset of symptoms occurred before the age of forty. All patients showed some degree of improvement, especially a decrease in the frequency of bowel movements and relief of abdominal cramps; gross blood in the stools was either much diminished or completely disappeared. There was a gain in weight in 14 patients which was most marked in adolescent and young adult patients. Basal metabolic rates were determined in 7 patients before and after the administration of the thiouracil drugs; only one of these patients showed a "gross" decrease in the metabolic rate; this patient also developed enlargement of the thyroid while taking thiouracil; another patient who showed diffuse swelling of the thyroid showed no significant change in the basal metabolic rate. Only one patient showed signs of toxicity — arthralgia and periarticular swelling which disappeared when the drug was discontinued. An increase in hemoglobin levels up to 6.5 Gm. per cent was noted; as the hydration of these patients improved as the diarrhea diminished, this indicates a definite improvement in the blood picture. As these patients were all ambulatory, other blood studies were not made. Proctosigmoidoscopic examination in 7 patients with active ulcerative colitis showed the rectal mucosa to be grossly normal following treatment; in 2 other patients, signs of active inflammation had disappeared, although a residual polypoid change persisted. In 5 patients x-ray studies were made during drug therapy; only one of these patients showed significant improvement; this patient had an ileostomy and an ileosigmoidostomy was

done after improvement under thiouracil therapy; he is now free from symptoms fourteen months after intestinal continuity was restored and fifteen months after thiouracil was discontinued. These results indicate that the thiouracil drugs have a definitely beneficial effect on chronic ulcerative colitis; it is suggested on theoretical grounds, that this may be due to the effect of these drugs on the parasympathetic nervous system.

COMMENT

A treatment well worth investigating.

M.W.T.

Use of Quinidine in Treatment of Chronic Auricular Fibrillation

E. H. Yount and associates (*A. M. A. Archives of Internal Medicine* 39:63, Jan. 1952) report the treatment of 155 patients with chronic auricular fibrillation with quinidine. The underlying condition responsible for the development of the arrhythmia was arteriosclerotic heart disease in 50 per cent and rheumatic heart disease in 30 per cent; in the remaining 20 per cent, thyrotoxicosis or various "miscellaneous conditions." The treatment resulted in restoration of normal sinus rhythm in 110 patients, or 75 per cent. The duration of the quindine therapy in these cases in which normal rhythm was restored varied from one to eighteen days, averaging 5.9 days. The average dose of quinidine at the time normal rhythm was restored was 0.42 Gm. given every four hours. In the patients in whom reversion to normal rhythm occurred, the plasma level of quinidine in most cases varied from 8 to 12 mg. per liter, averaging 9.1 mg. per liter at the time of the reversion. In 9 patients in whom the plasma level of quinidine reached 16 mg., only 4 were restored to normal rhythm. In cases with thyrotoxicosis, response to quinidine was unsatisfactory until the thyrotoxicosis was corrected; the auricular fibrillation then responded promptly to quinidine therapy in almost all cases. The response to quinidine therapy was much the same in cases of arteriosclerotic and rheumatic heart disease. The duration of the fibrillation did not affect the results of quinidine therapy, as patients with fibrillation of over two years' duration responded as promptly as those with fibrillation of less than six months' duration. Patients in the oldest age groups (seventy to eighty-six years) required the smallest dosage for satisfactory results. The most common side effects of quinidine therapy are gastrointestinal disturbances, which occurred in 30 per cent of the patients in this series; they were mild as a rule and did not make it necessary to discontinue therapy. Toxic reactions due to labyrinthine disturbances occurred in 15 per cent, but also were not severe enough to indicate discontinuance of treatment. "Precipitant hypotensive reactions" did not occur in any case in this series. No embolus occurred after restoration of normal rhythm in the 23 patients who showed definite evidence of previous emboli; and this complication occurred in only 2 patients during or after the administration of quinidine.

COMMENT

Well worth reading in its entirety.

M.W.T.

A Solution for the Parenteral Administration of Calcium

R. H. Hoffman and associates (*American Journal of Digestive Diseases*, 19:79, March 1952) report the use of a calcium preparation for parenteral injection in cases in which the serum calcium is below 10 mg. per cent. The preparation used is Calphosan (R), a specially prepared 1 per cent solution of calcium lactate and calcium glycerophosphate in normal saline with a pH of 7.2, which can be given by intragluteal injection without causing pain or induration. In most cases, it was found that the administration of four doses of 10 cc. each at weekly intervals was sufficient to raise the serum calcium level to above 10 mg. per cent, and to maintain

it at that level for the period of observation (nearly a year3. If the serum calcium fell below 9.5 mg. per cent, another series of four injections was given. In persons with normal serum calcium (above 10 mg. per 100 cc.), the injection of Calphosan (R) did not permanently affect the serum calcium level. The cases treated with Calphosan (R), included hyperinsulinism, hypothyroidism, menopausal disturbances, urticaria and bronchial asthma. In all these cases, raising the serum calcium to normal by means of this therapy resulted in "greater subjective well being."

COMMENT

Any one who has injected calcium intravenously and got it into the tissues, knows how painful it is. It is a relief to know that there is an effective preparation which can be used intramuscularly and without pain.

M.W.T.

SURGERY

BERNARD J. FICARRA, M.D.*

The Difficult Diagnosis of Early Gastric Cancer

E. A. Lawrence *(Journal of the Indiana State Medical Association,* 44:289, April 1951) has found that the demonstration of occult blood in the stool by the guaiac test after meat-free diet for three days is of aid in the early diagnosis of gastric cancer. A gastric analysis and blood count should also be done. If occult blood is found in the stools and gastric acidity is low in a patient who complains of "dyspepsia," a complete gastrointestinal examination should be done; this should include gastroscopy and cytological examination of gastric washings for malignant cells. As gastric cancer is frequently associated with pernicious anemia, all patients with pernicious anemia should be carefully watched and gastrointestinal x-ray examinations done periodically as an aid in the early detection of gastric cancer in this particular group. Gastric polyps are generally regarded as precancerous lesions and should be treated by subtotal or total gastrectomy, depending upon the extent of the polypoid disease. As gastric cancer may arise in gastric ulcer, especially in ulcers on the greater curvature and in the cardia, the author is of the opinion that such ulcers should be treated surgically; ulcers in the prepyloric region and on the lesser curvature should also be treated surgically if they do not heal under adequate medical management "in a reasonable period of time." In cases of suspected gastric cancer, operation is indicated unless the presence of distant metastases is demonstrated. If an early diagnosis of gastric cancer is made, and operation is done promptly before lymph node metastases have developed, the prognosis is good.



Ficarra

COMMENT

Dr. Lawrence calls attention to the early diagnosis of gastric cancer. It is most appropriate that he should do so, since this problem is always with us. Too frequently the surgeon at the time of operation finds an inoperable

* Diplomate American Board of Surgery; Associate visiting surgeon, Brooklyn Cancer Institute, St. Peter's Hospital (Head and Neck Service), Hospital of the Holy Family, Brooklyn.

carcinoma of the stomach and remarks, "If only we had operated upon this patient sooner." Early diagnosis is imperative for early surgery. Early surgery offers a more favorable prognosis. Therefore any information which will assist in the early diagnosis of gastric cancer is worthy of our attention.

B.J.F.

The Early Management of the Burned Patient

E. I. Evans *(Surgery, Gynecology and Obstetrics*, 94:273, March 1952) states that when a burned patient is first admitted to the hospital, the extent of the burn is mapped out, so that the extent of burn injury can be estimated with the use of a chart. If burn shock is established, a colloid solution is given immediately; the author has found that gelatin and dextran are as effective as pooled plasma in burn shock; if the burn is deep and involves more than 25 per cent of the body surface, whole blood is given as well as plasma or plasma substitutes. The hourly urine output and the initial hemoglobin must be determined, and a formula for the administration of plasma or plasma substitutes, whole blood, saline solution and glucose has been employed based on these findings; but even in extensive burns, more than 4000 cc. of 0.9 per cent sodium chloride is rarely required in the first twenty-four hours, and half this amount in the second twenty-four hours. After the first forty-eight hours, intravenous therapy is not usually required in burned patients, who can usually take adequate fluid and food by mouth by this time. In the treatment of burn wound, the author has recently employed a one piece burn dressing, which can be easily and quickly applied to the burn wound. Its inner surface is a dry fine mesh gauze applied directly to the burned area without grease or ointment; the intermediate layer is a one-inch layer of absorbent cotton and then many layers of cellulose treated to be water repellent. The outer layer is a non-woven cotton fabric also treated to be water repellent. This dressing is not removed until the twelfth or fourteenth day and at that time the burn wound is usually dry, and in the more superficial wounds, healing is well advanced at that time. In only one case treated by this method, the dry dressing stuck to the burn in an area of full thickness slough. The application of this absorptive dressing relieves pain promptly. This type of dressing is indicated chiefly in burns of the extremities and "encircling" burns of the trunk. An exposure treatment has been employed in some cases, chiefly burns of the face and perineum; no dressing is applied to the burn wound, the patient is placed on sterile sheets and protected from draft; a low environmental temperature with a high relative humidity is desirable for this type of treatment. Deep, full thickness burns require removal of the burn slough and skin grafting, whatever type of initial treatment is employed.

COMMENT

Any discussion on burns is always a welcome treatise. Burns remain one of the most difficult problems to manage in spite of the many contributions made during the past decade. Dr. Evans' mention of blood substitutes is worthy of emphasis, especially in a disaster area when plasma and large quantities of blood are needed.

B.J.F.

Terramycin in the Treatment of Peritonitis

Eric Reiss and associates *(A. M. A. Archives of Surgery*, 64:5, Jan. 1952) report the treatment of 68 cases of peritonitis with terramycin; 47 of these patients were treated at Brooke Army Hospital and 21 at Tokyo Army Hospital. In the Tokyo group, the peritonitis was secondary to gunshot wounds of the abdomen in all but 3 cases; in the Brooke Hospital group, peritonitis was secondary to appendicitis in 28 of the cases. In 31 of the 47 Brooke patients, terramycin was the first antibiotic employed, within forty-eight hours after the onset of the symptoms of peritonitis. In the Tokyo group, penicillin and streptomycin in combination had been used in "the forward areas" before the patients

had been sent to Tokyo. Terramycin was given intravenously (1 Gm. every twelve hours) for two to four days, then by mouth in a dosage of 0.5 Gm. every six hours for eight to ten days. The results of therapy were classed as excellent if the temperature fell to normal, peristalsis returned, and abdominal tenderness diminished in forty-eight to seventy-two hours; the results were classed as good when similar improvement occurred more slowly. In some cases recovery was good, but the role of the antibiotic was doubtful on account of the use of surgical drainage. The largest percentage of excellent results was obtained in the most virulent infection, i.e., in the cases of spreading peritonitis; in the 32 cases of this type, results were excellent in 17 cases, good in 8, poor in 6, and doubtful in one case; 4 of 5 patients with spreading peritonitis secondary to appendicitis did not require surgery. There were 2 deaths in this group, one in a case of spreading appendiceal peritonitis, and one in the case of peritonitis secondary to intestinal obstruction and gangrene; death in this case was probably due to thrombosis of a cerebral artery as shown at autopsy. In the other 4 cases with poor results, the organisms cultured from the wound were found to be terramycin-resistant; in 3 of these cases, chloramphenicol was used, and in one, streptomycin. In 18 cases of localizing peritonitis the results were excellent in 5 and good in 12 cases. In 12 cases of localized peritonitis results were excellent in 3 and good in 5 cases. In 6 cases of pelvic inflammatory disease with pelvic peritonitis, results were excellent in one, and good in 5 cases. The incidence of nausea and vomiting with oral administration of terramycin was low in this series, which is attributed to the fact that the antibiotic was routinely given with milk.

COMMENT

The experience of Doctor Reiss and his associates is corroborated by the experience of many surgeons in civilian practice. Even with the excellent administration of the antibiotic drugs, an occasional patient still dies from generalized peritonitis.

B.J.F.

Use of Gelatinized Bone in Skeletal Trauma

W. A. Swanker and J. M. Winfield (*American Journal of Surgery*, 83:332, March 1952) describe the preparation of gelatinized bone and report its use in 65 cases of skeletal defects of the face and extremities. When the defect is small, and little scar tissue is present, as in certain facial deformities, the gelatinized bone can be injected underneath the periosteum with a large gauge hollow needle. In other cases, the gelatinized bone is introduced by the open method. Most of the cases treated were skeletal defects about the face, including 27 cases of saddle-nose deformity, of which 23 were due to trauma, 18 cases of supra-orbital ridge defects due to trauma or extensive frontal sinus surgery (2 cases) and 10 cases of mandibular deformity. The results were good in all but one case of ununited fracture of the mandible, in which some of the gelatinized bone became deposited underneath the skin; the wound healed satisfactorily, but the scar was fixed and showed an irregular surface. The gelatinized bone was also employed in a few cases of bone defects in the lower extremities, with good results. In one of these cases, the knee joint was tuberculous, and showed bone absorption; autogenous gelatinized bone was used to obtain joint fusion; eleven months later, there was a severe injury to the knee, with a fracture line occurring below the fusion. The authors suggest that the use of gelatinized bone may be of advantage in cases of delayed union and ununited fractures, because of its stimulating effect on bone healing.

Pilonidal Sinus: An Evaluation of Plastic Closure Using Flaps of Gluteal Muscle

R. W. Dwight (*A. M. A. Archives of Surgery*, 64, 438, April 1952) reports 135 cases of pilonidal sinus in which the glu-

teal flap operation described by Shute, Smith, Levine and Burch in 1943 was employed. This method was used in these cases because many of the patients lived at a distance from the hospital and could not be treated as outpatients, and it was thought that this plastic closure of the wound would reduce the long period of hospitalization necessary for healing of an open pilonidal wound. During the same period 110 other patients with pilonidal sinus were admitted to the hospital, for whom this operation was considered unsuitable. Major wound infection occurred on the fourth to the eleventh postoperative day in 13, or 10 per cent of the 135 cases; in 6 of these cases, the wounds healed without reoperation, but the patients lost more time than they would have with any open operation. In the 127 patients who were followed up for a year or more there were 13 recurrences. Complications of a less serious nature, not requiring reoperation, occurred in 19 other cases. The difficulty in dealing with the cases of failure and recurrence after the gluteal flap operation, and the prolonged period of treatment required in these cases lead the author to conclude that this type of operation with extensive plastic closure is not indicated in the treatment of pilonidal sinus. In selected cases of small midline lesions, he employs minimal excision and closure without the use of plastic flaps, and open treatment in other cases of pilonidal sinus.

OPHTHALMOLOGY

RALPH I. LLOYD, M.D., F.A.C.S.*

Detection of Intra-ocular Tumors With Radioactive Phosphorus

C. I. Thomas and associates *(A. M. A. Archives of Ophthalmology*, 47:276, March 1952) report their preliminary studies on the use of radioactive phosphorus (p. 32) in the diagnosis of intra-ocular tumors. This radioactive isotope was selected for these studies because it is a beta-ray emitter and therefore considered more suitable for localization of tumors near the outer surface of the eye than a gamma-ray emitter. A small Geiger counter was used for determining the radioactive uptake. This method was found to be of special value in determining the cause of retinal detachment in questionable cases that did not show definite clinical evidence of fluid pressure or choroidal tumor. In the first case on which the test was used, there was a large area of retinal detachment but no visible tear, and the presence of a tumor was suspected. The radioactive phosphorus test was negative for tumor, but the eye was enucleated; the histologic examinaiton showed no evidence of tumor. In one other case of retinal detachment in which there was a tear in the retina and the clinical evidence was considered to indicate conclusively that the retinal detachment was due ot fluid pressure and laceration, the radioactive phosphorus test was used "for control pur-



Lloyd

* Consulting Ophthalmologist, Cumberland, Prospect Heights, Brooklyn Eye and Ear, Long Island College and Peck Memorial Hospitals, Brooklyn.

poses," and proved entirely negative. In 5 other cases in which an intra-ocular tumor was suspected, the radioactive phosphorus uptake indicated a malignant lesion; this was confirmed at operation in 4 of these cases; no operation was done in the fifth case. In another patient (case 8), there was a cyst in one eye which was infected; the other eye was normal; the Geiger count was higher in all parts of the infected eye than in the normal eye, but not higher in any one area of the eye (as in the cases of tumor). In all the cases in this preliminary study, the tumor was in the anterior portion of the choroid, but radioactive phosphorus uptake could also be measured in more posterior areas with rotation and fixation of the eye. While further study of radioactive phosphorus in the diagnosis of intra-ocular tumors is necessary, the results reported "provide strongly presumptive evidence" of its value.

COMMENT

Research of this type can only be done in laboratories equipped and manned in a way that is rarely found because of the expense and preoccupation of laboratory staffs in more important routine work.

It is hoped that more money will be given in the future for advanced types of research such as this.

R.I.L.

Intra-ocular Acrylic Lenses: A Recent Development in the Surgery of Cataract

Harold Rilley *(British Journal of Ophthalmology*, 36:113, March 1952) reports the use of an artificial lens in 27 cataract operations. The first cases were carefully selected, the operation being done only if the cataract was "completely monocular"; later the selection of cases was "less stringent." The artificial lenses used are made of fully polymerized polymethyl methacrylate (Transpex I), cut in dimensions about 1 mm. less than the dimensions of the human lens; the refractive power of the lens in a medium with the refractive index of the aqueous fluid is + 24D. A groove is cut in the circumference so that the lens can be grasped by forceps, and special forceps have been designed for this purpose. Extracapsular extraction is usually employed, but in 2 of the cases in this series, an intracapsular extraction was done successfully. The acrylic lens can be inserted at the time of the cataract extraction, if the posterior capsule has been completely cleared before the corneo-scleral sutures are tied; in 3 cases the eye was closed after cataract extraction and the acrylic lens inserted several weeks later. In the first 2 cases the acrylic lens was too thick; in the first case no corneo-scleral sutures were used and iris prolapse developed; the eye is now quiet and both this patient and the second patient operated on have "moderate" visual acuity but only with the use of spectacles. Only one of the other 25 has any trouble with the lens and in this case, the operative wound healed slowly. In the other 24 cases binocular vision is better than it is following the usual cataract operation. In these cases, the lens is in good position, with normal intra-ocular tension and no active inflammation. In some cases, exudate and iris pigment on the lens partially obstruct vision, but in all these cases there has been definite improvement, and it may be that all will become clear, and the visual acuity of the eye improve still further.

COMMENT

The plan of placing a foreign body in the place usually occupied by the lens, with the iris in front and the ciliary body around it, is so at variance with previous experience that the average oculist would not think of doing it. Nevertheless, some very good results have been reported and the tolerance of the eye to the substitution of an artificial lens demonstrated for a considerable period. The final word will not be said for some time yet.

R.I.L.

A New Vasodilator in Ophthalmology

J. J. Stern *(American Journal of Ophthalmology*, 35:187, February 1952)

reports the use of priscoline as a vasodilator in 5 cases, including 3 cases of angiospastic process in the retina, one case of optic neuritis and one case of neuroparalytic keratitis. In all these cases, Priscoline was given by mouth in tablets of 25 mg. each, three to four times a day. Nausea was severe in only one case and this was controlled by the use of sodium bicarbonate; other side effects of Priscoline —hot flashes, chilliness, formication — were of only slight degree. In the 3 cases of retinal angiospasm, the treatment resulted in practically complete clearing up of the lesions in 2 cases, and marked improvement in the third case, although the focus in the retina was still visible. In the case of optic neuritis, the nervehead became completely normal in appearance, with no enlargement of the blindspot; several months after treatment was discontinued a follow-up showed the same normal condition. In the case of neuroparalytic keratitis, the condition appeared to be "an isolated process," no other local and no systemic pathological condition being found. Vision in the right eye was almost completely lost (perception of light and dark only) and vision in the left eye was 20/40; under Priscoline treatment vision in the left eye improved to 20/25 and there was some improvement in the right eye, with some clearing of the opacities. Pain had been entirely relieved, and the eyes were quiescent. In this case, the eye lesion was undoubtedly "a progressive process," in which progress was halted and the process even partly reversed by treatment with a vasodilator. In the other cases reported, there seems to have been "a common angiospastic component" in either the arterioles or larger blood vessels, so that vasodilator therapy was effective. Vasodilator therapy is not effective in every case, as it failed in 2 case of occlusion of the central retinal artery and in other cases of senile degenerative processes.

COMMENT

Potent remedies of the type used can be administered only under proper supervision. It is also to be mentioned that as striking results have been obtained by other methods.

R.I.L.

Systemic and Laboratory Investigation of Intra-ocular Disease

N. L. Hart *(New Orleans Medical and Surgical Journal* 104:372, March 1952) reports 27 cases of uveitis at a Veterans Hospital, in which in addition to a complete ophthalmological examination, otolaryngological, dental and complete physical examinations were made. The latter included urinalysis, stool and sigmoidoscopic examinations, serological tests for syphilis, the tuberculin test, and tests for brucellosis, tularemia, typhoid and paratyphoid. In 10 of these patients the stool or sigmoidoscopic examination showed the presence of *E. histolytica*. When these patients were treated for the amebic infection with aureomycin or terramycin or with carbarsone and chiniofon until the organisms disappeared from the stools, the eye condition cleared up promptly, sometimes "dramatically." In 1 patient in whom the Wassermann test was positive for syphilis, it became negative under adequate penicillin therapy, but the uveitis did not subside until *E. histolytica* disappeared from the stools under treatment with carbarsone and chiniofon. This series is too small to permit a definite conclusion that there is "a casual relationship" between uveitis and intestinal amebiasis, but the fact that the eye condition responded in every case of amebic infection to adequate amebicidal therapy appears to be "more than simple coincidence"; and indicates the value of complete physical examination including stool examinations, in the study of intraocular disease. Cortisone acetate was used locally in a number of the cases in this group, as soon as the patient was first seen, while the complete etiologic study was being made. Cortisone does not act on the etiological agent, but "holds" the ocular response to the systemic disease in

abeyance," until the nature of the underlying disease is determined and appropriate treatment instituted, and its use may be continued as an adjuvant to such treatment.

COMMENT

It is not surprising that amebic diseases should produce eye disease like uveitis. In certain parts of the world intestinal diseases of the types produced by amebic disease are almost certain to affect newcomers. The so-called tourist disease of Mexico demonstrates the lack of sanitation as it is understood here. When war service takes men to many strange and poorly supervised places, many infections follow and when these men return, a strange group of tropical diseases are seen.

R.I.L.

Clinical and Pathological Characteristics of Radiation Cataract

D. G. Cogan and associates (*A. M. A. Archives of Ophthalmology*, 47:55, Jan. 1952) report a clinical study of 20 cases of radioation cataract in an early stage; and a histological study of 27 radiation cataracts removed at operation. In the 20 clinical cases, the cataract followed exposure to x-rays or gamma rays in 7 cases; cyclotron exposure in 2 cases; exposure to atomic bomb explosions in Japan in 12 cases, and exposure to an atomic explosion in the United States in one case. The findings in all these cases were "remarkably uniform." The initial opacity, as seen with the ophthalmoscope, was "a dot," usually in the posterior pole of the lens, which gradually increased in size; as the opacity developed it showed a relatively clear center resulting in a doughnut-shaped pattern. With slit-lamp biomicroscopy, the initial opacity was found to be granular and usually of a yellow color; the earlier opacities were on the posterior capsule; as the opacity developed the slit lamp biomicroscope showed its anterior boundary to be sharply demarcated and that it had a bivalve configuration. These findings are "strongly suggestive" that a cataract is of the radiation type, and usually serve to differentiate radiation cataract from posterior pole cataract and cataracta complicata. Of the 27 cataracts studied histologically, the cataract was caused by radiation therapy of a tumor in or near the eye in 24 cases, in 2 cases resulted from exposure to an atomic bomb explosion, and in one case from cyclotron exposure. The chief histological changes found in these cataracts were piling up to the equatorial cells and failure of these cells to differentiate into lens fibers; and the early migration of cells toward the posterior pole of the lens beneath the posterior capsule, which may cause thickening of the capsule. Many of the histologic changes observed in these cases may occur in other types of cataract; and the authors are of the opinion that the histologic findings in radiation cataract "are less type specific than are the clinical signs."

COMMENT

This is a most valuable contribution. Radiation cataract is rare but a very important matter because of the increasing use of various forms of radiation.

R.I.L.

Urology Awards

The American Urological Association offers an annual award of $1000.00 (first prize of $500.00, second prize $300.00 and third prize $200.00) for essays on the result of some clinical or laboratory research in Urology. Competition is limited to urologists who have been in such specific practice for not more than five years and to men in training to become urologists.

The first prize essay will appear on the program at the forthcoming meeting of the American Urological Association, to be held at the Hotel Jefferson, St. Louis, Missouri, May 11-14, 1953.

For full particulars write the Executive Secretary, William P. Didusch, 1120 North Charles Street, Baltimore, Maryland. Essays must be in his hands before January 15, 1953.

MEDICAL BOOK NEWS

Anesthesiology

Chloroform. A Study After 100 Years. Edited by Ralph M. Waters, M.D. Madison, University of Wisconsin Pr., [c. 1951]. 8vo. 138 pages, illustrated. Cloth, $2.75.

Chloroform, by Dr. Waters, provides a very valuable protocol and outline for pharmacologic research in anesthesia and other specialties. This book scientifically dispels much of the prejudice and superstitions which have grown up around this drug over the years, and more important it instills a healthy respect for the discriminating use of all drugs, chloroform in particular. For all who prescribe or administer drugs this book is a must. The moral contained in this book is that an anesthetic is only as safe as the administrator.

IRVING M. PALLIN

Radiology

An Atlas of Normal Radiographic Anatomy. By Isadore Meschan, M.D. With the assistance of R. M. F. Farrer-Meschan, B.S. [Melbourne, Australia]. Philadelphia, W. B. Saunders Co. [c. 1951]. 4to. 593 pages, illustrated. Cloth, $15.00.

This is a very fine text. It makes an interesting and valuable source book for experienced radiologists. It should be prescribed reading for radiologic students, residents, and technicians. It belongs on every radiologist's shelf.

The line drawings are excellent. It is too bad that the radiologic reproductions are of such poor quality, but this is the fault of the publisher, not the author.

MORTIMER R. CAMIEL

Medicine

Differential Diagnosis of Internal Diseases. Clinical Analysis and Synthesis of Symptoms and Signs. By Julius Bauer, M.D. New York, Grune & Stratton, [c. 1950]. 8vo. 866 pages, illustrated. Cloth, $12.00.

This book is a very readable and rather complete text. It has been arranged in two parts which quite equally divide the volume. Part One is a compilation of "Leading Symptoms" and Part Two of "Leading Signs."

At the end of each chapter there is an adequate summary and a voluminous bibliography.

In general, the reviewer considers this an interesting and worthwhile text of differential diagnosis. While it is not as complete as many standard volumes on medicine, it may be used profitably as a ready reference.

A. SIDNEY BARRITT, JR.

Clinical Pathology

Clinical Laboratory Methods. By W. E. Bray, M.D. 4th Edition. St. Louis, C. V. Mosby Co., [c. 1951]. 8vo. 614 pages, illustrated. Cloth, $7.25.

This fourth edition includes the recent contributions to the practice of clinical pathology. Some of the new subjects added, are: the new nomenclature of the blood cells; bone marrow findings; anemias; prothrombin consumption test; Rh-sensitized red blood cells; insulin and epinephrine tolerance tests; adrenocorticotropic hormone; liver function tests;

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methods for concentrating tubercle bacilli; tests for rickettsia; agglutinins in atypical pneumonia; recent antibiotics; etc. The text is concise and is well illustrated. On the whole, it is a very valuable book for both laboratory worker and clinician.

EDWARD H. NIDISH

Biography

A Doctor's Pilgrimage. By Edmund A. Brasset, M.D. Philadelphia, J. B. Lippincott Co., [c. 1951, The Author]. 8vo. 256 pages. Cloth, $3.50.

This is an interesting story, full of absorbing incidents. Not a story of "From Rags to Riches;" but it can be titled "From Rags to the Riches of Contentment."

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I closed the book with a feeling of high regard for the doctor and with the knowledge that his patients are receiving the benefits of a competent and conscientious doctor, two ingredients of equal importance.

S. R. BLATTEIS

Histology

Essentials of Histology. By Margaret M. Hoskins, Ph.D. & Gerrit Bevelander, Ph.D. 2nd Edition. St. Louis, C. V. Mosby Co. [c. 1952]. 8vo. 240 pages, illustrated. Cloth, $4.00.

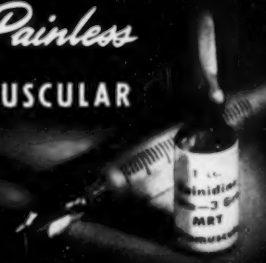
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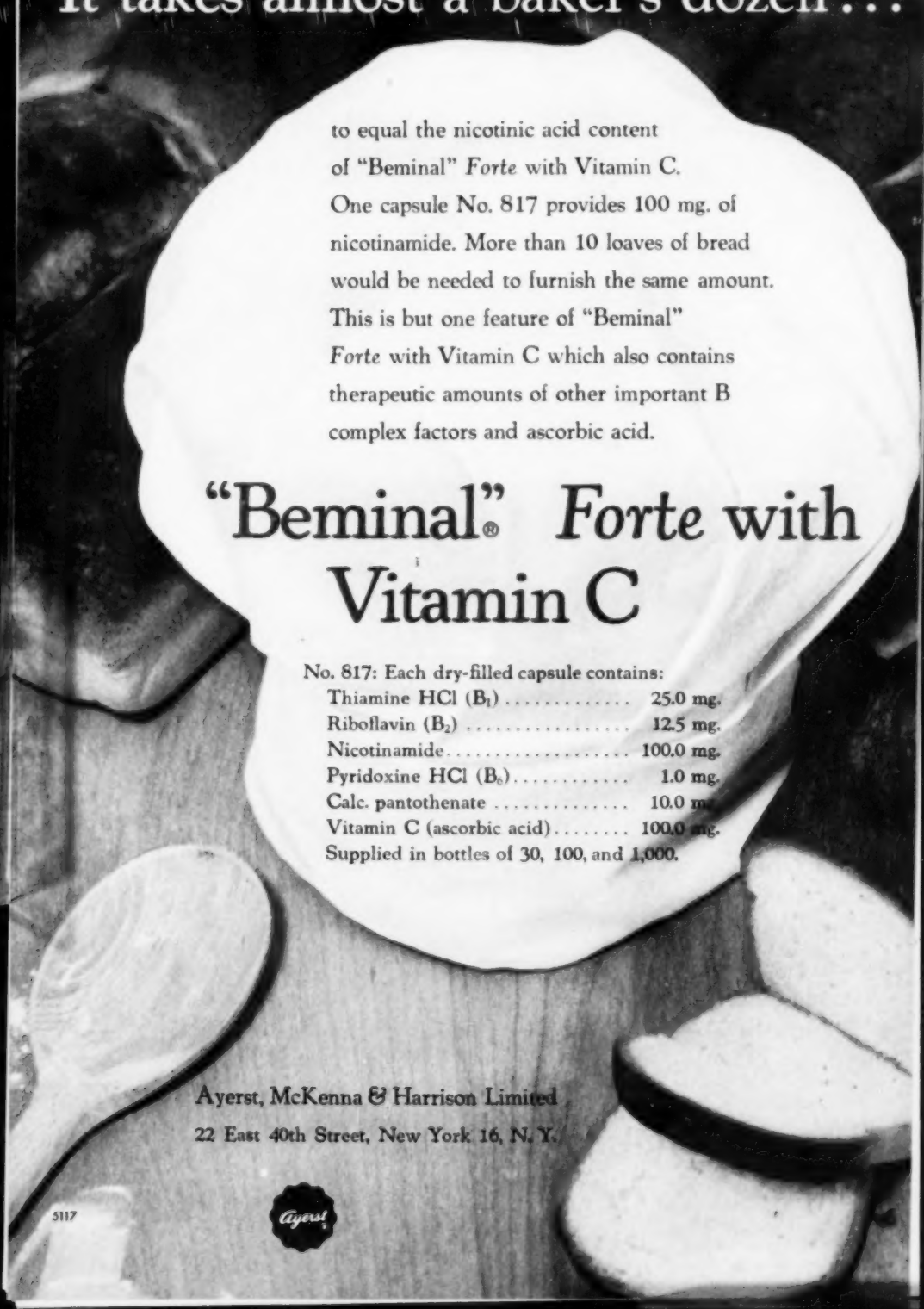
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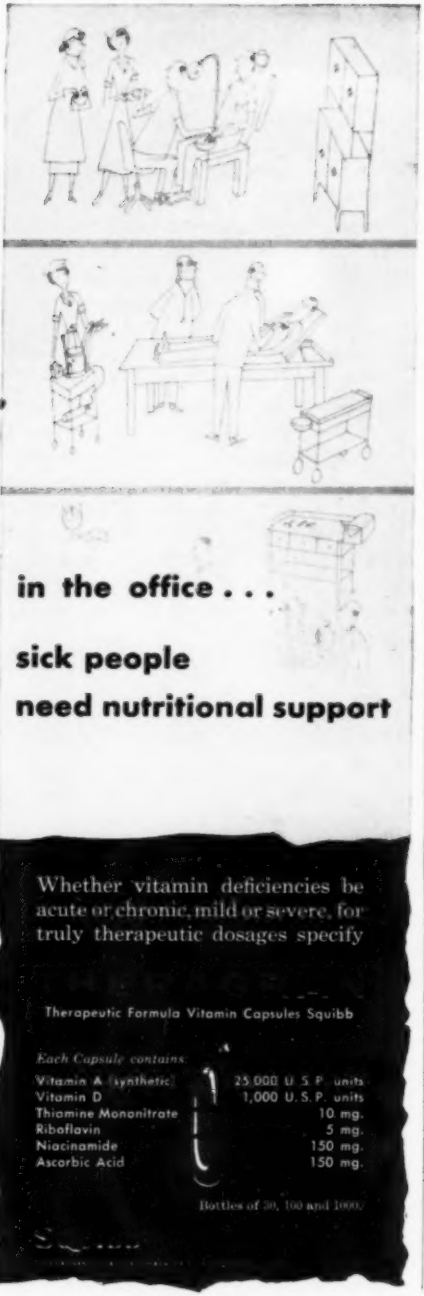
Use of Ion Exchange Resins in Edema

Anion-cation exchange resins proved to have a synergistic effect along with the mercurical diuretics in 3 of 4 patients with incapacitating edema resulting from congestive heart failure. The mercurial diuretics alone proved to be ineffective in these patients. However, one patient developed low salt syndrome and one developed potassium depletion. The author suggested that the reason for the synergistic action might be due to the fall in the plasma CO_2Cl ratio. Best also reported in *Am. Pract. Digest Treat.* [3:274(1952)] that symptomatic improvement was obtained by the administration of the ion exchange resins in 3 patients with edema due to chronic glomerulonephritis, intercapillary glomerulosclerosis complicated by diabetes mellitus, and congestive heart failure attended by irritability of the myocardium. The mercurial diuretics were contraindicated in each of these patients.

The resins used in this study were Carbo-Resin (12 per cent anion exchange resin, 29 per cent cation exchange resin in the potassium cycle and 59 per cent cation exchange resin in the hydrogen cycle), Natrinil (a cationic exchange resin of the carboxylic type, 80 per cent hydrogen cycle and 20 per cent potassium cycle), and Resodec (a mixture of ammonium and potassium carboxylic exchange resins).

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MODERN THERAPEUTICS

—Continued from preceding page

Neomycin Sulfate in Different Ointment Bases

Neomycin sulfate, in a concentration of 5 mg. per Gm. of ointment, was used in the treatment of 115 patients with impetigo, folliculitis, impetignized eczematous dermatitis, and bacterial paronychia. Myciguent, a base containing mineral oil, wool fat, and petrolatum, was used on 39 patients, a cream base containing Tegacid regular (glyceryl monostearate combined with a sapamine salt), polysorbate 80, propylene glycol, spermacet, methylparaben, and water was used in treating 48 patients, and a water-miscible base containing Carbowax 4000, Carbowax 1500, Tween 20, and Propylene glycol was used in the treatment of 28 patients. Forbes reported in *South. Med. J.* [*45*:235(1952)] that the infections were cleared in from 2 to 10 days when the ointments were applied three times a day. He found that the results with Myciguent and the cream base were superior to those obtained with the water-miscible base. He also found that patients infected with hemolytic streptococcus or with pseudomonas required longer treatment than those infected with hemolytic staphylococcus.

Evaluation of Methylparafynol As a Hypnotic

Methylparafynol (Dormison) represents a new class of hypnotics in having only carbon, hydrogen and oxygen in the molecule. It was administered to a series of 134 patients by Chevalley *et al.*, who reported in *N. Y. St. J. Med.* [*52*:272 (1952] that oral doses as capsules or elixir of 100 to 400 mg. a day were given for periods ranging from 2 to 120 days. The usual effective dose was about 300 mg. but, in a few cases this dose was repeated 3 times at intervals of 2 hours.

No side effects were observed or reported by the patients even with the large repeated doses.

The drug produced a hypnotic effect in less than one hour in the majority of patients and was also metabolized quickly. The latter fact reduced hangover symptoms the next morning. Methylparafynol produced sleep in patients not experiencing pain or mental tension. Therefore, the authors concluded that the drug probably has its greatest usefulness in patients with simple insomnia.

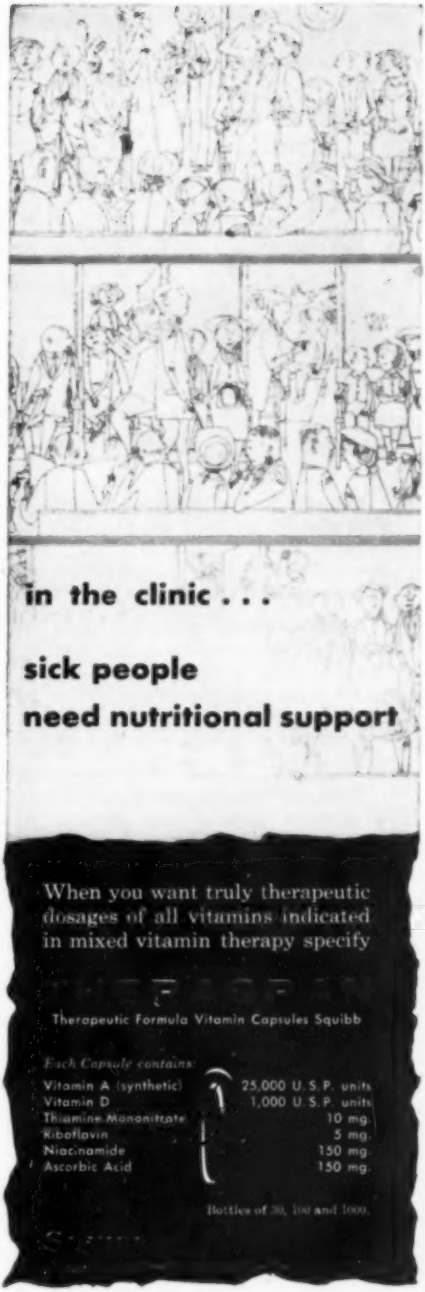
Therapeutic Use of Alpha-Tocopherol Acetate in Kidney Disease

Sixteen children with glomerulonephritis, ranging in age for 23 months to 12 years, were treated orally with 30 to 100 mg. of alphatocopherol acetate per day. Some also received 0.5 Gm. of ascorbic acid per day, and 11 severely ill children also received 6 injections of 10,000 or 20,000 units of penicillin. Prosperi reported in *Riv. clin. pediat.* [*50*:39 (1952)] through *Squibb Abst. Bull.* [*25*:703 (1952)] that all of the children were clinically cured after 4 to 26 days of therapy. There was a decrease in temperature and a disappearance of hematuria within 3 to 4 days after the start of therapy and an increase in diuresis after the first 24 hours. The 11 children given the treatment, combined with the penicillin, recovered in an average of 14 days after therapy had started, and the others recovered in an average of 9 days. The alphatocopherol acetate was continued for ½ to 1 month after the clinical cure was achieved.

Therapeutic Use of Terramycin in Nonspecific Urethritis

Thirty selected male patients with nonspecific urethritis who were refractory to routine therapy were also refractory to 1 or more antibiotics given orally or parenterally. Subsequent dilatation of the urethra and instillation of 10 per cent mild

—Continued on following page





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Castle **LIGHTS AND STERILIZERS**

—Continued from preceding page

silver protein at weekly intervals for 3 months resulted in cures in 18 patients. Ferguson and Miller reported in *J. Urol.* [*67*:762 (1952)] that 10 of the remaining 12 patients were cured by the weekly or semi-weekly intra-urethral instillations of 10 cc. of a 5 or a 2.5 per cent solution of terramycin hydrochloride, when accompanied by dilatation and massage of the urethra.

The authors also reported that 66 of 72 similarly refractory cases were cured with 1 to 5 treatments at weekly or semi-weekly intervals. The treatments were composed of intraurethral injections of 2.5 per cent terramycin hydrochloride solution with dilatation and massage of the urethra.

Antagonism of Vitamin K to Anticoagulants

The slow intravenous administration of an emulsion of vitamin K_1, mixed with freshly drawn blood, or 5 per cent dextrose in water, was found to be safe and effective in reversing excessive hypoprothrombinemia due to the experimental administration of dicoumarin or certain other anticoagulants. Single doses of 50 mg. in 25 patients, and single doses of 75 to 500 mg. in 8 patients, were effective in returning the prothrombin time to normal in all but 1 patient, irrespective of the hypoprothrombinemia or the amount of depressor drug which had been given. The results were not consistent in 9 patients given 5 to 40 mg. of vitamin K_1. Rehbein, Jaretzki, and Habif reported, in *Ann. Surg.* [*135*: 454 (1952)] that no bleeding due to coagulation defect occurred in 7 patients receiving preoperative anticoagulant therapy who were given 50 mg. vitamin K_1 prior to operation. When dicoumarin was given 6 to 48 hours after 50 mg. of vitamin K_1 the anticoagulant response was normal in 9

—Continued on page 76a



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Each Kapseal contains:

Taka-Diastase (Aspergillus Oryzae Enzymes)	2½ gr.
Vitamin B_1 (Thiamine Hydrochloride)	10 mg.
Vitamin B_2 (Riboflavin)	10 mg.
Vitamin B_6 (Pyridoxine Hydrochloride)	0.5 mg.
Vitamin B_{12} (Cyanocobalamin)	1 mcg.
Pantothenic Acid (As the Sodium Salt)	3 mg.
Nicotinamide (Niacinamide)	10 mg.
Vitamin C (Ascorbic Acid)	30 mg.
Liver Concentrate N.F.	0.17 Gm.
Liver Fraction No. 2 N.F.	0.17 Gm.

In bottles of 100 and 1000.



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Each teaspoonful (4 cc.) contains:

Taka-Diastase (Aspergillus Oryzae Enzymes)	2½ gr.
Vitamin B_1 (Thiamine Hydrochloride)	2 mg.
Vitamin B_2 (Riboflavin)	1 mg.
Vitamin B_6 (Pyridoxine Hydrochloride)	0.5 mg.
Pantothenic Acid (As the Sodium Salt)	2 mg.
Nicotinamide (Niacinamide)	5 mg.

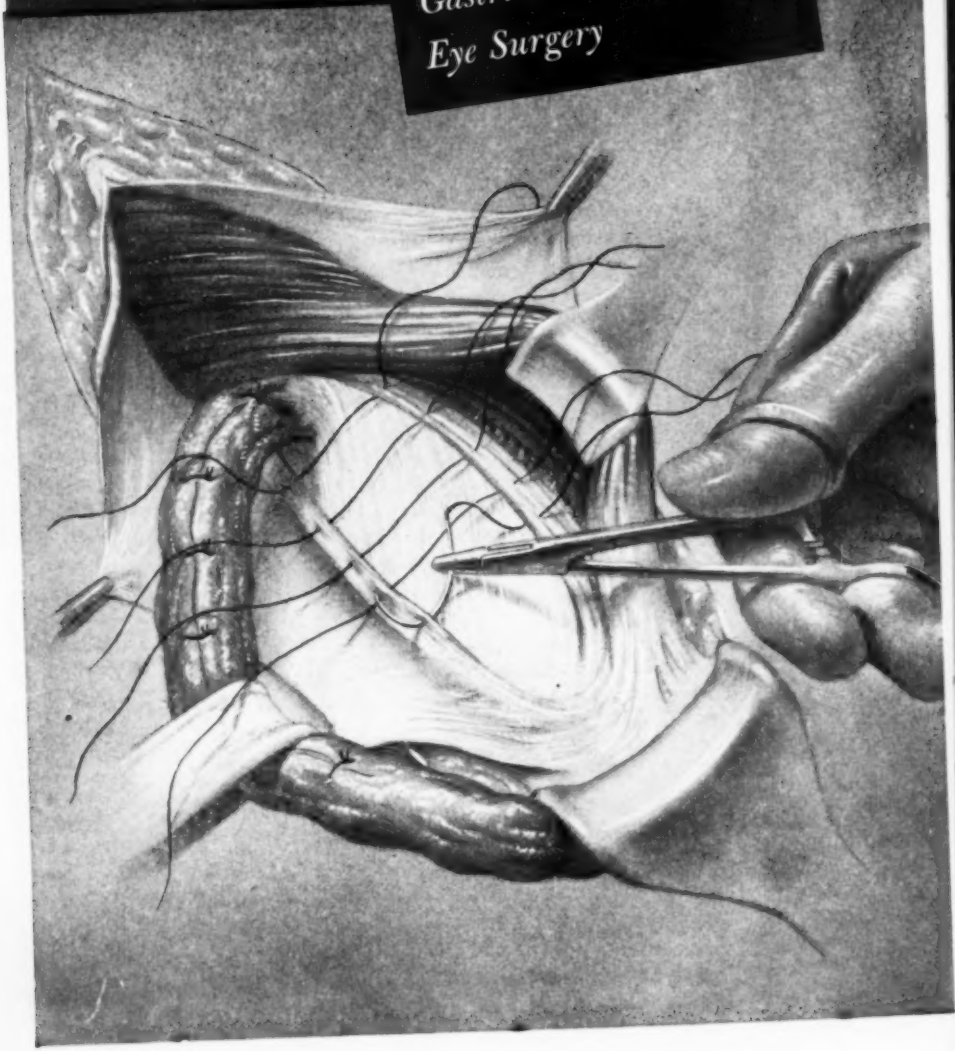
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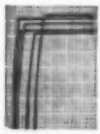
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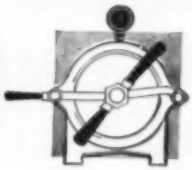
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patients but was poor after 150 to 200 mg. in 1 of 2 patients.

Experiments on Motion Sickness Prevention

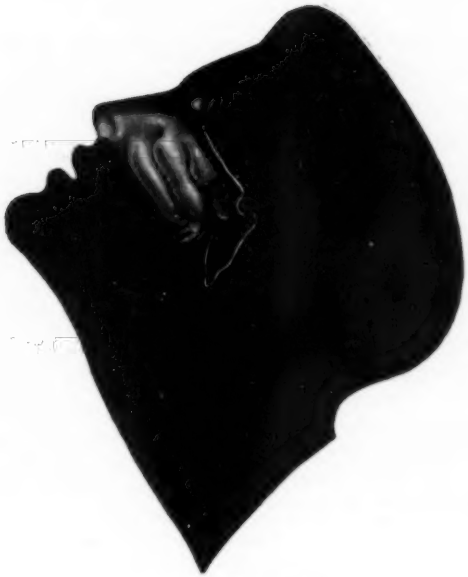
Hyoscine hydrobromide 1 mg., phenergan 35 mg., hyoscine 1 mg. and phenergan 25 mg., hyosine 0.65 mg. and phenergan 15 mg., and the latter combination plus mannitol hexanitrate 50 mg. were compared for their effectiveness in the prevention of motion sickness. Vomiting or nausea was evident in 11 per cent of the men given hyoscine alone, in 27 per cent given phenergan alone, ranged from 7 to 14 per cent given the combinations, and was 57 per cent among the men when given a placebo. A total of 150 men participated in the experiments.

Glaser and Hervey, writing in *The Lancet* [*262*:490 (1952)], stated that hyoscine definitely gave better results than phenergan alone, but that no definite conclusions could be drawn from the results with the combinations as to any greater effect. The authors also found that 30 per cent of those made seasick the previous day were protected when the hyoscine was given only 5 to 10 minutes before boarding the float. This compared with 78 per cent protected when the hyoscine was given 1¼ hours before boarding time.

Neomycin Therapy in Amebiasis

Four of 7 patients with amebiasis caused by *E. histolytica* were cured with a single course of Neomycin totalling 1,600,000 units. The 3 remaining patients were cured by an additional course of therapy in which 4,800,000 units of Neomycin were given. All of the patients showed rapid healing of amebic ulcerations and disappearance of the para-

—Continued on page 78a



prolonged relief from nasal congestion within 2 minutes with just 2 drops of



Privine® hydrochloride **0.05 %**

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potent, prompt-acting Privine is a virtually nonirritating nasal vasoconstrictor which can be administered to children as well as adults.

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—Continued from page 76a

sites and all of the patients remained free from *E. histolytica* for a 3-month observation period following the termination of therapy.

McVay, Laird, and Stern reported in *The Am. J. Med. Sci.* [223:20 (1952)] that the only significant toxic reaction observed as a result of therapy with Neomycin was a transient rise in the protein level in urine and an elevation of blood protein and blood urea nitrogen in one patient. However, the authors pointed out that further investigation of the toxicity of Neomycin should be undertaken before its use on a wide scale. They noted also that there was an enormous increase in the yeast cells in the whole series of patients. This reaction is thought by some to be an important cause of the nausea, vomiting, and diarrhea often associated with the administration of Neomycin.

Purified Pectin as a Plasma Extender

A specially prepared pectin sol has been shown to be effective in shock therapy as a plasma extender. Baier stated that the pectin sol has also been found to be safe, inexpensive and of good stability. There is slight transitory enlargement of the spleen after large quantities of pectin have been infused but no toxic lesions developed. Pectin was found to be largely eliminated with the urine. It was also stated in *Nutrition Res.* [8:2 (1952)] that the pectin sol corrected abnormally long bleeding time and that polygalacturonide degration products had a detoxifying effect.

The special pectin sol is prepared by autoclaving a solution of N.F. pectin. This reduces the molecular weight of the pectin to approximately that of the blood protein. This sol is then made isotonic, filtered,

—Continued on page 81a

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ASTERIC Brewer (5 gr. enteric-coated Aspirin) will be found beneficial for those patients suffering from hemorrhagic gastritis resulting from the irritating effects of plain aspirin and for cases of peptic ulcer which require acetylsalicylic acid therapy.

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*Talkov, R. H., Ropes, M. W., and Bauer, W.: *The Value of Enteric Coated Aspirin.* N.E.J. Med. 242,19 (Jan. 5) 1950.

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—Continued from page 78a

packaged and then again lightly sterilized, all at the normal pH of pectin of about 3.8. This sol is quite stable. It is diluted with a buffer to bring the pH of the sol to about 6.5 just prior to use.

A new methoxyl pectin, capable of forming a gel without sugar, has been used in the preparation of diabetic jellied fruit desserts.

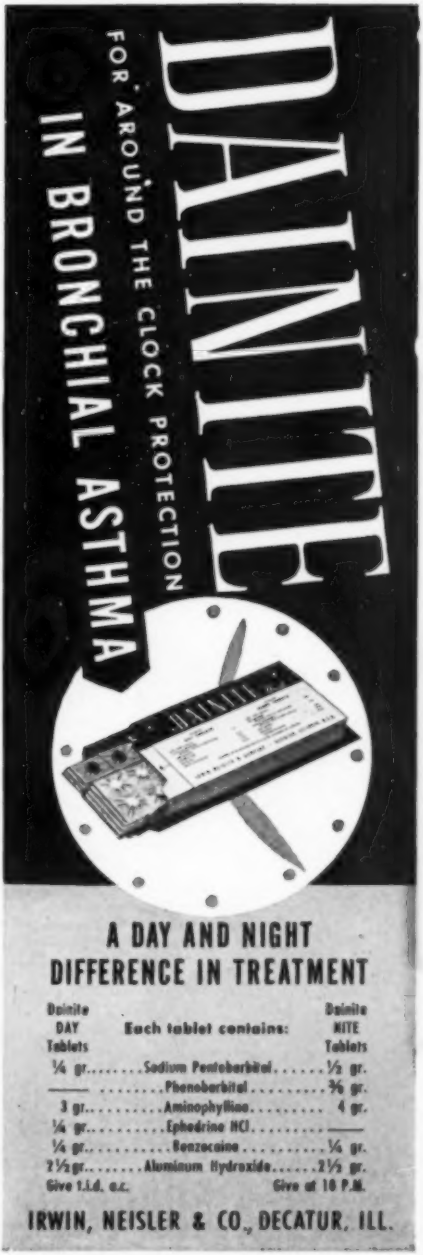
Veratrum Viride in Toxemias of Pregnancy

Vergitryl (a purified Veratrumviride extract) was employed in the treatment of hypertensive toxemias of pregnancy. The intramuscular route was employed for the nonconvulsive type of toxemias. 0.75 unit of Vergitryl was mixed with 1 cc. of 1 per cent procaine and given at once. This dose was repeated whenever the blood pressure was over 140/90, every hour if necessary. If no hypotensive effect was obtained at the end of one hour the dose was increased to 0.9 unit.

The intravenous route was employed for treatment of the convulsive type of toxemias. In this treatment 1.5 units of Vergitryl was mixed with 20 cc. of 5 per cent dextrose and given at the rate of 1 cc. per minute until the first 20 mm. fall in systolic or 10 mm. fall in diastolic pressure occurred. Additional Vergitryl, at ½ the original dose, was given whenever the blood pressure rose to 140/90 or above. This treatment was continued through labor and delivery and for the first 24 hours after delivery or until the blood pressure became stable or the signs and symptoms of toxemia disappeared.

According to Finnerty in *New England J. Med.* [*246*:646(1952)], excellent results were obtained in 92 of 114 nonculvulsive toxemia patients, good results in

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19, fair results in 3, and a poor result in 1. Excellent results were also obtained in 4 to 8 patients with convulsive toxemia, good results in 2, and fair results in 2 patients. Vomiting, the only toxic manifestation observed, was effectively controlled in the 21 patients exhibiting this symptom by the intravenous administration of 50 mg. of pentobarbital sodium. There were 2 fetal deaths and no maternal deaths in this series.

Treatment of Poisoning With Barbiturates

The treatment of poisoning by barbiturates with a simple routine was discussed by Locket and Angus in *The Lancet* [*262*: 580 (1952)]. A total of 64 patients, varying from comatose to conscious, were admitted and treated. A lavage of 2 pints of normal saline or tap water was given promptly. The patients then received 500,000 units of penicillin intramuscularly every 6 hours until they had been conscious for 48 hours. This was employed because of the high incidence of bronchopneumonia in this type of patient. Oxygen was administered continuously at a rate of about 10 liters per minute until respiration was normal, cyanosis had disappeared and consciousness had been fully restored.

The authors reported that only 2 of the comatose patients died out of the 64 patients treated.

Sulfadiazine in Nongonococcal Urethritis

An increasing prevalence of a completely penicillin-resistant form of nongonococcal



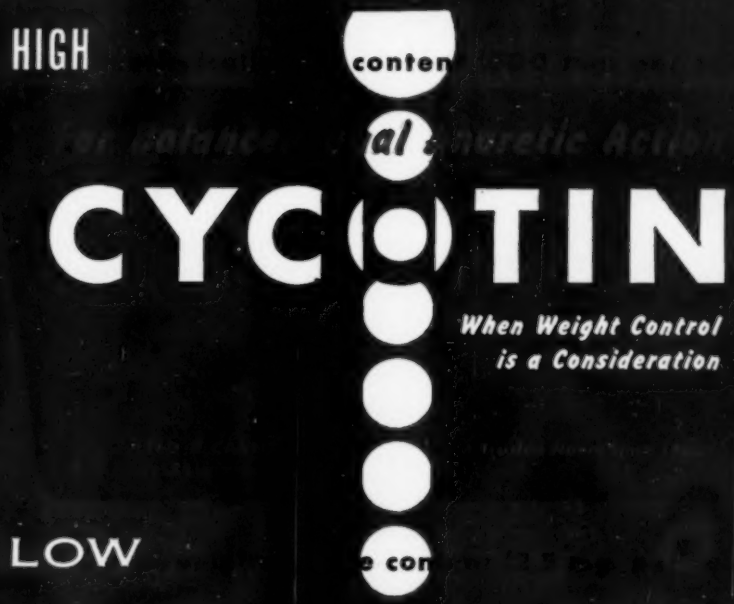
urethritis has been reported by the Armed Forces. The rather widespread substitution of pencillin as a prophylactic for mechanical prophylastic measures against venereal diseases may be a contributing factor in this development, according to Graham, writing in the *U.S.A.F. Med J.* [3:401(1952)].

Chloramphenicol was moderately effective and was used in patients in whom a limited or excessive loss of fluid was anticipated as a result of field duties. Aureomycin was less effective than chloramphenicol and, as already mentioned, penicillin was completely ineffective. However, sulfadiazine was effective in 90 per cent of 1,000 cases in which it was given. The dosage required was an initial dose of 4 Gm. followed by 1 Gm. every 4 hours. No drug was effective, however, unless "milking down" of the urethra, excessive fatigue, sexual intercourse, and alcoholic beverages were avoided.

Parenteral Administration of Calcium

A 1 per cent solution of calcium lactate and calcium glycerophosphate (Calphosan) having a pH of 7.2 was injected intragluteally in doses of 10 cc. once a week for 4 doses. In 8 patients having low blood calcium levels the preparation brought about a rise in the calcium level to about 10 mg. per 100 cc., which is considered to be normal. This level was maintained for almost a year in most of the patients, without further treatment. However, the initial series of 4 injections was repeated at least once in 5 of the patients because of insufficient early response.

Hoffmann, Abrahamson and Josephson reported in *Am. J. Digest. Dis.* [*19*:79 (1952)] that the injections produced no indurations or sloughs. As was expected, no effect on the serum calcium levels was observed in patients already having normal levels.



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NEWS AND NOTES

Blood Vessel Dilating Drug Helps Prevent Amputation of Gangrenous Limbs

To reduce the need for amputation in cases of gangrene and ulceration caused by poor circulation in the extremities, Priscoline may be used, according to a clinical investigation reported in *Angiology* (April 1952).

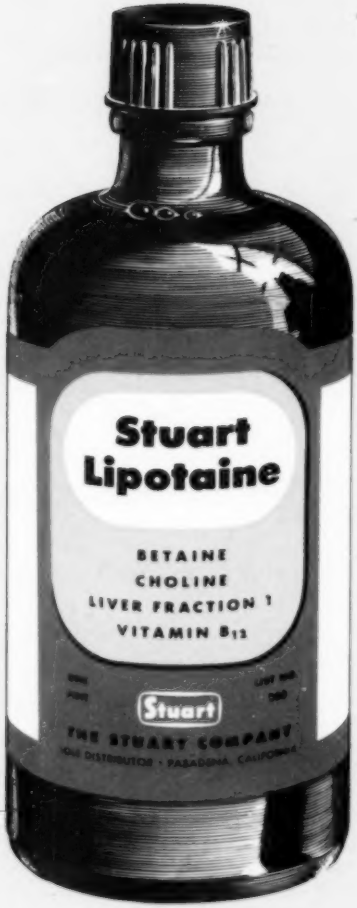
The investigation was conducted by Dr. Heinz I. Lippmann at Montefiore Hospital, New York City, over a period of three years. Eighty cases of peripheral vascular diseases, including patients with arteriosclerosis, cardiac conditions and diabetes were studied.

Dr. Lippmann reported that out of a group of 22 patients with gangrene of the heel, 11 were treated with Priscoline while the remaining 11 received conventional therapy. Of the 11 treated with Priscoline, eight recovered without amputation. In the group of 11 who did not receive Priscoline, only two recovered without amputation.

Commenting upon the results, Dr. Lippmann reported, "The healing of ischemic heel lesions after prolonged intermittent intra-arterial Priscoline treatment, in addition to proper management, constitutes the most tangible achievement of this form of therapy to date."

A further group of patients suffering from gangrene or ulceration, most of whom had been referred to the hospital for amputation, was given prolonged intra-arterial Priscoline treatment. Although the average age of this group was high and most were in poor general condition, Dr.

This is the first lipotropic product to provide the advantages of betaine in addition to choline, liver and B12 in a pleasant-tasting liquid or an easy-to-swallow capsule



Stuart

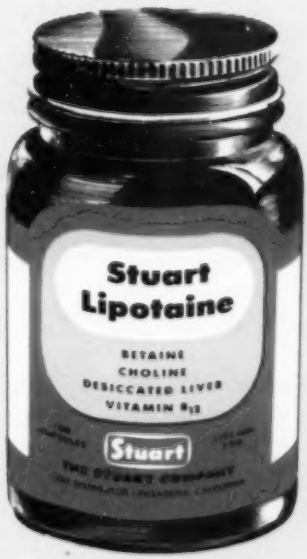
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Betaine* . . . (3000 mg.)	3 Gm.
Choline*	210 mg.
Liver Fraction 1 N.F. . .	210 mg.
Vitamin B_{12} (USP Crystalline) . .	12 mcg.

EACH CAPSULE contains:

Betaine*	333 mg.
Choline*	35 mg.
Desiccated Liver N.F. . .	35 mg.
Vitamin B_{12} (USP Crystalline) . .	2 mcg.

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1. 5 mg. Dextro-Amphetamine Sulphate to inhibit appetite
2. ¼ gr. Phenobarbital to offset nervous stimulation
3. 200 mg. Methylcellulose to provide needed bulk
4. 9 Vitamins* } to provide protective amounts of important nutrients
5. 8 Minerals*

*Vitamins: A, 1700 USP units; D, 170 USP units; C, 25 mg.; B_1, 1 mg.; B_2, 1 mg.; Niacin Amide, 10 mg.; B_6, 0.15 mg.; B_{12}, 1 mcg.; Calcium Pantothenate, 1.5 mg. Minerals: Calcium, 40 mg.; Phosphorus, 30 mg.; Iron, 3 mg.; Copper, 0.25 mg.; Iodine, 0.05 mg.; Cobalt, 0.167 mg.; Manganese, 0.33 mg.; Zinc, 0.1 mg.

Stuart

Lippmann reported that 20 cases healed without any amputation, and the degree of surgery required was minimized in an additional three cases, so that only local amputation of a toe was necessary. In the majority of these cases Priscoline was reported to be apparently the main factor responsible for the favorable results.

The study also included the use of Priscoline in treating four patients with Raynaud's disease who had failed to respond to conventional treatment. The attacks were reported to have disappeared during, and for some time after, the Priscoline treatment. Equally satisfactory results were achieved with the treatment of four patients suffering from ilio-femoral thrombophlebitis with spastic arterial occlusion. Rapid improvement with one or few intraarterial Priscoline injections was noted although the course of the circulatory disease was not influenced.

In summing up the results of his studies, Dr. Lippmann concluded that if "intra-arterial Priscoline treatment is judiciously used, it is a valuable adjunct in the management of peripheral vascular disorders."

Effect of Thephorin upon Primary Dysmenorrhea

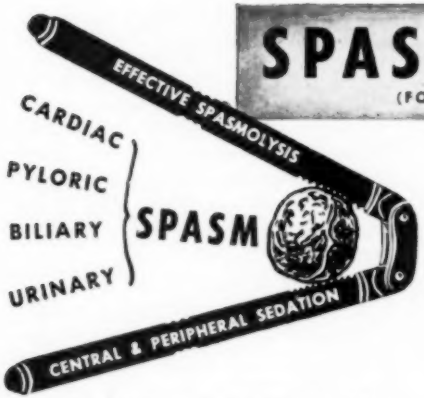
"Thephorin therapy for symptomatic relief in primary dysmenorrhea appears to be safe, practical, convenient and economical," according to Maietta writing in *Annals of Allergy* [*10*:34, May-June (1952)].

Patients selected for this study were between the ages of thirteen and forty-two; sixteen women were single and four married. Nineteen had a history of allergy, including asthma, hay fever, allergic coryza, eczema, urticaria and angioneurotic edema. Organic causes of dysmenorrhea were ruled out in all instances.

—Continued on following page

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Contains hyoscine hydrobromide, homatropine methyl bromide and aprobarbital (allyl-isopropyl-barbituric acid). Spasmanol provides effective spasmolysis that is markedly free from side reaction, and potentiated by relatively non-cumulative sedation of both central and peripheral nervous systems.

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Most physicians are opposed to harsh laxatives except for occasional use. Habitual constipation is best treated by a natural regulator, **CHOLOGESTIN.**

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CHOLOGESTIN restores regularity by stimulating the flow of Nature's laxative, healthy bile. Its digestant action aids protein and fat digestion.

•

Indicated for chronic constipation in patients past 35, and in all cases where a **choleretic** or **cholagogue** is in order. Average dose, 1 tablespoonful after meals.

•

Formula contains ox bile extract compounded with therapeutic adjuvants (sodium salicylate, pancreatin and sodium bicarbonate). Also available as Tablogestin (Tablets of Chologestin), 3 tablets equivalent to 1 tablespoonful.

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Gentlemen: You may send me without obligation a professional sample of Tablogestin Tablets, together with literature on Chologestin.

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NEWS AND NOTES

—Continued from preceding page

With the onset of pain a 25 mg. tablet of Thephorin was administered. This dose was repeated in one-half to two hours if relief was not obtained. Further medication was taken at four-hour intervals if indicated. Two doses were usually adequate. Thephorin was selected by Maietta because of its "low sedative quotient."

The author observes that placebos administered to each patient at suitable intervals were "strikingly ineffective and the dysmenorrhea was not relieved." When Thephorin was administered the following month, "the symptoms were completely controlled." Antihistaminic therapy had no effect on the flow.

The author presents four typical case histories which illustrate the results obtained in all twenty cases receiving antihistamine therapy. He states that Thephorin "gives prompt and effective relief, can be taken orally, is attended by minimal and inconsequential side reactions, improves morale and allows a continuance of normal activities."

Diet to Lose Weight Must be Medically Supervised

Don't lose your health trying to lose weight.

This warning was issued by Dr. Max Millman of Springfield, Mass., who stated that "the treatment of obesity, like that of any other important abnormality of the human body, calls for sound medical supervision."

Writing in a recent issue of *Today's Health*, published by the American Medical Association, Dr. Millman said the first and most common pitfall in reducing is the careless choice of a diet. As the modern treatment of obesity is based primarily on the restriction of caloric intake, the obese person should avoid at all times any and all dietary fads, regardless of

their claim of origin, as they are as dangerous as they are useless.

"Obesity is recognized today as a major public health problem," he pointed out. "It predisposes its victims to a long list of complications, including diabetes, heart disease and high blood pressure. It shortens life to a shocking degree. Its immediate elimination is imperative and urgent.

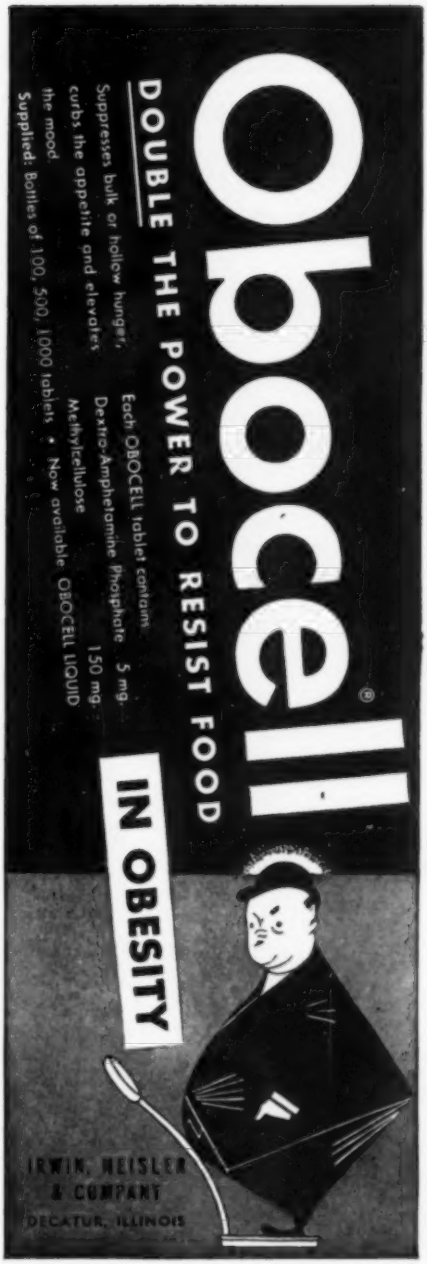
A weight loss of one to three pounds a week is sufficient, according to Dr. Millman. It is not sufficient to count calories alone, but it is also necessary to make sure that the diet contains an adequate amount and variety of proteins, minerals and vitamins. A good and adequate diet, whether it is designed for the lean, or fat, or in-between, must include representatives of the following basic seven groups of food:

1. Green and yellow vegetables.
2. Oranges, tomatoes, grapefruit — or raw cabbage or salad greens.
3. Potatoes and other vegetables and fruits.
4. Milk and milk products—fluid, evaporated, dried milk or cheese.
5. Meat, poultry, fish or eggs—or dried beans, peas or nuts, or peanut butter.
6. Bread, flour and cereals—natural whole grain or enriched or restored.
7. Butter and fortified margarine (margarine with added vitamin A).

All diets must be calculated according to the individual's needs, including calculations of the patient's age, occupation, degree of obesity, and the desirable rate of weight reduction, he added.

Dr. Millman warned against any diets which promise quick weight loss, as sudden or rapid loss of weight may impair health to a marked degree by lowering strength and resistance. The principle of such diets is starvation, which results in weakness, hunger and irritability. The few pounds lost under such conditions usually are regained quickly, and the person

—Continued on following page



—Continued from preceding page

not infrequently reaches the false conclusion that all dietary methods of weight reduction are useless and hopeless.

"There is no reducing chemical or drug known to medical science which is safe enough for anyone to take without strict and competent medical supervision. It is because of this that patent medicine manufacturers in recent years have been forced by federal agencies to exclude all such chemicals and drugs from their products.

"The result is that no patent medicine on the market is capable of causing any weight reduction whatever."

The unwise use of exercise in weight reduction by the obese is dangerous, difficult, impracticable and ineffectual, especially in people of middle age or above, Dr. Millman said. In the later stages of reducing, when the main bulk of fat has been shed, exercise carried out wisely under the guidance and supervision of a physician gives tone to the muscles and helps to improve stamina and endurance of the patient. But in the early stages of treatment, or when obesity is marked, physical exercise is a dangerous waste of time.

Clinician Terms Lipotropics "Anti-Senescence Factor"

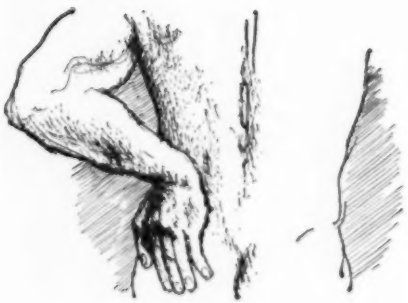
Lipotropic substances, in the form of Methischol, were administered as a major form of therapy in 86 elderly patients with such unrelated conditions as cirrhosis of the liver, precordial pain, leg pains, gallbladder disease, diabetes, etc. The "common denominator" in this series of unrelated cases was hypercholesterolemia, with various symptoms of arteriosclerosis exhibited.

—Continued on page 90a

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and other rheumatic diseases

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COUNCIL-ACCEPTED BRAND OF MEPHENESIN

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HERMANN, E. F. and SMITH, R. T.: The Journal-Lancet 71:271, 1951

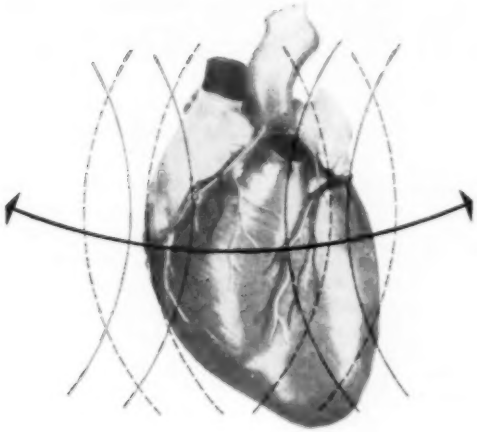
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TABLETS: 0.5 Gm./ELIXIR: 0.1 Gm. per cc.

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when maintenance dosage is see-sawing...

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chief active principle of digitalis purpurea for positive, controlled maintenance

Initial compensation of the failing heart may now be accomplished in hours rather than days — but maintenance of the compensated state is often a regimen of years. Continuous adjustment of the daily cardiotonic dose, which may contribute to patient morbidity, is often obviated when a preparation of reliable, constant and unvarying potency is employed.

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DIGITALINE NATIVELLE is available, at all druggists, in three strengths for precise dosage — 0.1 mg. (Pink), 0.15 mg. (Blue), 0.2 mg. (White). Because of the high order of purity, most patients are adequately maintained on 0.1 mg. daily. The average dose for digitalization is 1.2 mg. in three equal doses at 4-hour intervals.

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NEWS AND NOTES

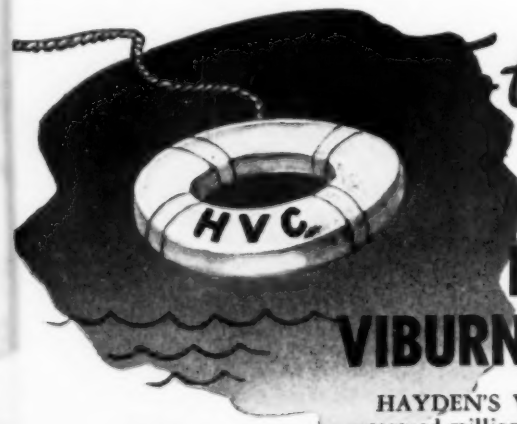
—Continued from page 88a

Abrahamson observed "striking and dramatic effects." It is difficult, he writes, in *Am. J. Digestive Dis.* [June (1952)], "to maintain enough sicentific objectivity to restrain one's enthusiasm. We may have in these lipotropic substances, an 'Anti-senescence factor,' for many of these patients were saved from obsolescence and were enabled to continue in useful pursuits." Long-standing and troublesome symptoms were relieved, the patients felt better in general as imrpovement in hepatic sufficiency occurred and serum cholesterol descended toward the normal. There appeared less tendency towards the extension of the arteriosclerotic process.

Typical of the more difficult cases treated was an alcoholic patient with cirrhosis of the liver who had been ill for several months with marked prostration, enormous abdominal swelling and ascites. Following treatment with Methischol and other therapy, Abrahamson stated, "This startling case shows the efficacy of the lipotropic substances in mitigating the toxic effects of alcohol on the liver and circulation. While he has been taking these drugs he has given no evidence of liver failure . . . His health is excellent. He is alert, vigorous."

Abrahamson suggests the advisability of routine serum determinations in every patient over 40 and the administration of lipotropic agents whenever the level is over 200 mg. per 100 cc. The preparation he used, Methischol, is a complete lipotropic formula containing methionine, choline, inositol, vitamin B_{12} and liver extract.

—Continued on page 92a



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r DYSMENORRHEA

HAYDEN'S VIBURNUM COMPOUND

HAYDEN'S VIBURNUM COMPOUND has rescued millions from loss of time in the home, office or factory. Prescribed extensively for the relief of functional dysmenorrhea, intestinal cramps, or *any smooth muscle spasm,* HVC has proven its effectiveness over many years of usage.

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(Isolated from ear infections and found resistant to antibiotics in laboratory tests)

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Urea	2.0 GRAMS
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RECTALGAN — Liquid . . . For symptomatic relief in:

—Continued from page 90a

Electric Insecticide Vaporizing Devices May be Dangerous

A warning against improper and excessive use of electric vaporizing devices for insecticides was issued in a report by the Committee on Pesticides of the American Medical Association and in an editorial, both appearing in a recent issue of *Journal of the A. M. A.*

Abuses of such devices have resulted in a number of cases of insecticide poisoning, the committee's report stated. Technologic improvements and methods of dispersal of such chemicals as DDT, benzene hexachloride, their isomers, and lindane have not been accompanied by parallel advances in knowledge of the physiologic actions of the insecticidal ingredients, particularly with respect to the hazards of chronic toxicity, inhalation, and food contamination, the report said, adding:

"While brief or occasional exposure [to such chemicals] appears to be harmless, it is not reasonable to expect that human beings can avoid injury if they are exposed for longer periods years after year to a toxic agent in atmospheric concentrations that kill insects in a few hours.

"It is further advanced that the resultant injury may be cumulative or delayed, or simulate a chronic disease of other origin, thereby making identification and statistical comparison difficult or impossible.

"The danger of substituting other more toxic chemicals when insect resistance to presently used compounds occurs, the

—Continued on page 94a

Randamin 'B'

Each 3 capsules contain:

Choline dihydrogen citrate	300 mg.
Inositol	150 mg.
Vitamin B_1 (Thiamin HCl)	75 mg.
Vitamin B_2 (Riboflavin)	36 mg.
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MASSIVE DOSAGE
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plus
CHOLINE & INOSITOL

for Geriatric Patients
for Treatment of:
Impaired Liver Function
Atherosclerosis
as Adjunctive Therapy in Diabetes
to Correct Endocrine Imbalance
as an Adjunct to Antibiotic Therapy

References: 1. New and non-official remedies, 1948, p. 426; Beams, A. J.: J. A. M. A. 130:190 (Jan. 26) 1946; Morrison, L. M.: J. A. M. A. 134:673 (June 21) 1947; Steigmann, F.: J. A. M. A. 137:239 (May 15) 1948.
2. Morrison, L. M.: Am. Heart J. 36:473 (Sept.) 1948.
3. Jukes, T. H.: Annual Review of Biochemistry, 1947.
4. Biskind, M. S. and Schrier H.: Report, N.Y. Acad. Med., (June) 1947.
5. Biskind, M. S.: J. Clin. Endocr. 3:227, 1943.

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"IN CURBING APPETITE and causing weight loss, a combination of Monobasic amphetamine phosphate containing a ratio of 1:3 of levo to dextro amphetamine (as found exclusively in Biphetacel) is more effective than the same amount of amphetamine contained in the racemic form where the ratio is 1:1 l/d . . ."*

Because of its exclusive 1:3 l/d ratio, Biphetacel curbs appetite more effectively, without nausea or nervousness, in both vagotonic or "sluggish" and sympathicotonic or "high strung" patients. In addition, it preserves an "enough-to-eat" feeling by decreasing gastric motility and prolonging emptying time of stomach, and assures normal elimination by supplying evenly distributed, non-nutritive, "no clump" bulk. Small dosage means low treatment cost.

Each Biphetacel tablet contains the preferred 1:3 l/d ratio as provided by Racemic Amphetamine Phosphate Monobasic 5 mg. and Dextro Amphetamine Phosphate Monobasic 5 mg.; Metropine® (methyl atropine nitrate, Strasenburgh) 1 mg., Sodium Carboxymethylcellulose 200 mg.

Dosage: 1 tablet ½ hour before meals, three times daily, for the vagotonic type. Increase this dose, if necessary, to achieve the desired clinical results. ½ tablet ½ hour before meals, three times daily, for one week for the sympathicotonic type. If no signs of intolerance develop, increase to 1 tablet. Supplied in bottles of 100 and 1000 scored tablets.

For literature and supply for initiating treatment, write Medical Service Department, R. J. Strasenburgh Co., Rochester 14, N. Y.

*Freed, S. C. and Mixel, M.—in press

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NEWS AND NOTES

—Continued from page 92a

temptation to relax sanitary precautions, and the lack of adequate justification for use in the light of these factors are additional reasons for viewing with concern the expanding use of vaporizing devices in human environment."

Use of such electrical devices for the intermittent or continuous dispersion of insecticides into the atmosphere of commercial establishments and homes has become popular during the last few years because of their convenience in the control of flying insects, the editorial pointed out.

Development data obtained under controlled conditions with certain of the machines indicated that amounts of poison were dispensed that neither deposited in significant quantities on exposed surfaces nor accumulated in the atmosphere of properly ventilated areas sufficiently to cause injury to humans exposed for ordinary working periods, the editorial stated, adding:

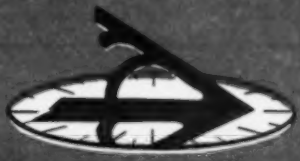
"It was found under practical conditions of use, however, that the laboratory standards for safe and effective performances were not being duplicated in practice. Poor construction and installation of units, tampering to effect greater control, overheating that resulted in excessive output, substitution of chemicals and formulas other than those recommended, installation in homes where overexposure to young children was likely, and a variety of other abuses have occured.

"These are fostered in part by exaggerated claims for efficiency and harmlessness and in part by a growing tendency of users to increase the output of the machines in order to control resistant strains of insects."

The use of make-shift dispensers should be discouraged, according to the committee's report. If it is necessary to use

—Concluded on page 96a

"Adoption of these control measures now is warranted by the evidence so far obtained" . . .



Now Therapeutic or Prophylactic Management in

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CORONARY DISEASES

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Each capsule supplies the true lipotropics (choline and inositol) approximately equivalent to one gram—choline dihydrogen citrate, also Vitamin A and the B-Complex factors, together with rutin and Vitamin C in adequate amounts.

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● The Gericaps formula makes possible a double use (Prophylactic and therapeutic) in the management of conditions of impaired metabolism of fat and cholesterol.

The lipotropics in Gericaps enter into the bio-synthesis of phospholipids, helping to bring about a better *balanced ratio* of cholesterol and phospholipids, which has been suggested as more important than the actual cholesterol level itself.

The low fat and cholesterol diet indicated is supplemented with adequate vitamins in the Gericaps formula, to compensate for the possible deficiencies caused by this restricted diet.

Gericaps contain therapeutic amounts of the factors to combat capillary weakness (rutin and Vitamin C) so often associated with abnormal cholesterol and fat metabolism.

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—Concluded from page 94a

any dispenser, only those which protect against fire hazard, excessive vaporization and the chemical alteration of the insecticidal ingredients because of high temperatures should be employed. The committee warned against the use of such devices in homes and sleeping quarters.

Low Hemoglobin Levels Probable in 6 Million Women

An estimated six million of the nation's 47,000,000 women between the ages of 18 and 59 years may have low hemoglobin (the oxygen-carrying red pigment of the red blood corpuscles) levels, according to an article in a recent *Journal of the A. M. A.*

The estimate was based on a study of persons disqualified as blood donors by the American National Red Cross. The study involved 239,191 white persons from various sections of the country who volunteered to donate blood from January, 1948, to June, 1949, inclusive. Of the group, 165,408 were men and 73,783 women.

A total of 13,798 men were disqualified, 1,382 (0.8 per cent) due to low hemoglobin levels. Of the women who volunteered, 15,233 were disqualified, including 9,322 (12.6 per cent) because of low hemoglobin levels. Recent spot surveys have shown no change in the situation, the article stated.

"Anemia is bound to be a subject of increasing medical interest if expansion of blood program operations should be continued, broader segments of the population included, and donor recruitment directed more intensely to women than at present."

The disqualifications were relatively more numerous during the most prevalent ages for child bearing and care, and less numerous among younger women and those in their late forties and fifties, the article stated.

The article was prepared by George W. Hervey, Sc.D., Ross T. McIntire, M.D., and Virginia Watson, M.S. All are associated with the national headquarters of the American National Red Cross, Washington.

Geriatrics Society to Publish Periodical

The American Geriatrics Society announces that effective with January 1953 they will publish their own official periodical to be called *The Journal of the American Geriatrics Society*. Dr. Willard Thompson, of Chicago, is President of the Society and will edit the journal. Dr. Melford Thewlis of Wakefield, R. I., is Permanent Secretary. All physicians interested in diseases of the aging are invited to join the society.

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an outstandingly safe and effective antibiotic combination in the management of skin infections
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Physicians	Equipment
Locations	Practices
Equipment	FOR RENT
Books	MISCELLANEOUS

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—Concluded on page 98a

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Mild mucus solvent for nose and throat



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BECK-LEE portable E.K.G. complete in carrying case, also the Mobile stand for cardiograph-4 leads. In perfect condition. Price $250.00 FOB Denison, Texas. Box 10G119, Medical Times.

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OFFICE, 3-room, for specialist. Furnished, near subway. New York. Rent: $50.; Service: $25.; Total: $75.00. Write Box 10R52, Medical Times.

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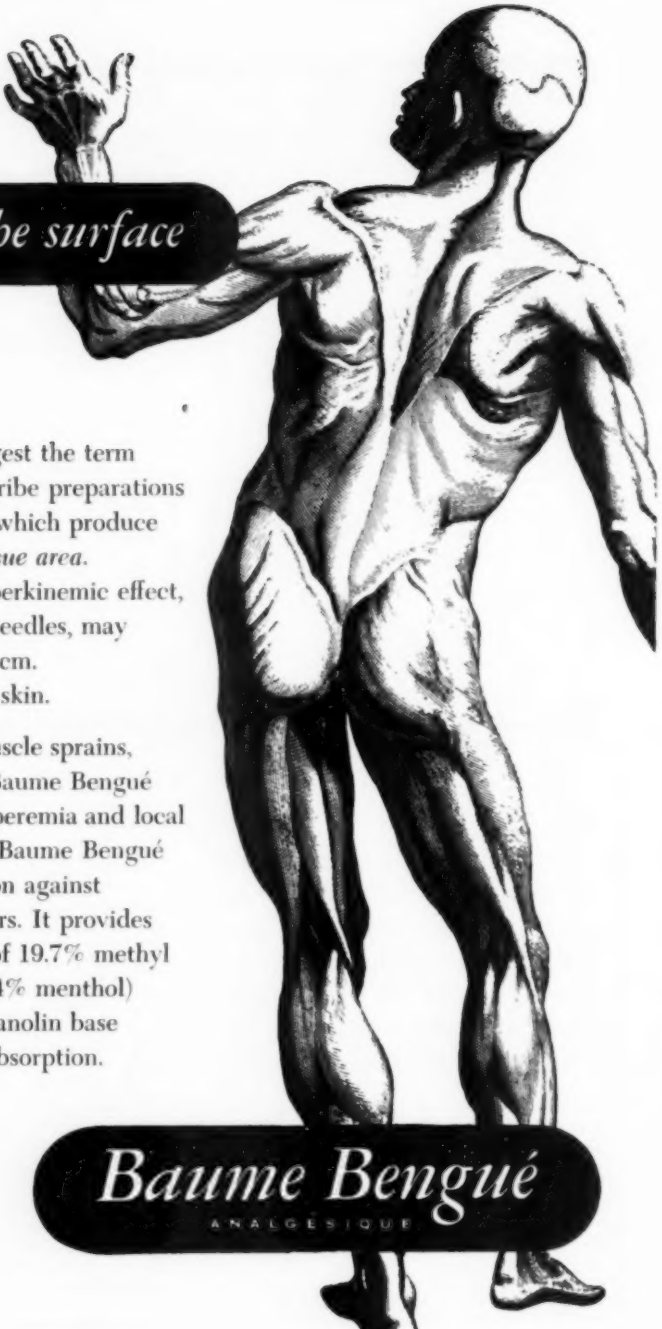
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1. Lange, K., and Weiner, D.: J. Invest. Dermat. 12:263 (May) 1949.

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1. Butterman, R.C.: Modern Medicine, 19:59 Dec. 15, 1951.

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